This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- CÓLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.



(43) International Publication Date 19 December 2002 (19.12.2002)

PCT

(10) International Publication Number WO 02/100851 A2

(51) International Patent Classification⁷: C07D 333/40, 413/04, 409/12, 409/04, 409/14, 495/04, 417/14, 413/12, 471/10, 417/12, 417/04, A61K 31/38, A61P 31/12, A61K 31/20

(21) International Application Number: PCT/CA02/00876

(22) International Filing Date: 11 June 2002 (11.06.2002)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/296,731

11 June 2001 (11.06.2001) US

- (71) Applicant (for all designated States except US): SHIRE BIOCHEM INC. [CA/CA]; 275 Armand-Frappier Blvd., Laval, Québec H7V 4A7 (CA).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): CHAN, Chun, Kong, Laval [CA/CA]; 27 Levere Street, Kirkland, Québec H9J 3X8 (CA). BÉDARD, Jean [CA/CA]; 437 Lansdowne, Rosemère, Québec J7A 3G6 (CA). DAS, Sanjoy, Kumar [IN/CA]; 553, 2ième rue, Laval, Québec H7V 1H7 (CA). NGUYEN BA, Nghe [CA/CA]; 175 Leotable Dubuc, LaPrairie, Québec J5R 5M5 (CA). PEREIRA, Oswy, Z. [CA/CA]; 12 Daudelin, Kirkland, Québec H2J 1L8 (CA). REDDY, Thumkunta, Jagadeeswar [IN/CA]; 2130 Scott, #127, St-Laurent, Québec H4N 1T2 (CA). SIDDIQUI, M., Arshad [CA/US]; 840 Memorial Drive,

Cambridge, MA 02139 (US). WANG, Wuyi [CA/CA]; 2297 Frenette, Ville St-Laurent, Québec H4R 1M3 (CA). YANNOPOULOS, Constantin [CA/CA]; 55 Poncelet, Ile Perrot, Québec J7V 8X3 (CA).

- (74) Agents: OGILVY RENAULT et al.; Suite 1600, 1981 McGill College Avenue, Montreal, Québec H3A 2Y3 (CA).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

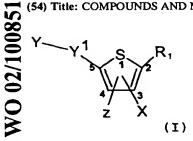
Published:

 without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

<

(54) Title: COMPOUNDS AND METHODS FOR THE TREATMENT OR PREVENTION OF FLAVIVIRUS INFECTIONS



(57) Abstract: The present invention provides novel compounds represented by formula I: or pharmaceutically acceptable salts thereof useful for treating flaviviridae viral infection.

COMPOUNDS AND METHODS FOR THE TREATMENT OR PREVENTION OF FLAVIVIRUS INFECTIONS

FIELD OF THE INVENTION

5

The present invention relates to novel compounds and a method for the treatment or prevention of *Flavivirus* infections using novel compounds.

10 BACKGROUND OF THE INVENTION

Hepatitis is a disease occurring throughout the world. It is generally of viral nature, although there are other causes known. Viral hepatitis is by far the most common form of hepatitis.

15 Nearly 750,000 Americans are affected by hepatitis each year, and out of those, more than 150,000 are infected with the hepatitis C virus ("HCV").

HCV is a positive-stranded RNA virus belonging to the Flaviviridae 20 family and has closest relationship to the pestiviruses that include hog cholera virus and bovine viral diarrhea virus (BVDV). HCV is believed to replicate through the production of a complementary negative-strand RNA template. Due to the lack of efficient culture replication system for the virus, HCV particles 25 were isolated from pooled human plasma and shown, by electron microscopy, to have a diameter of about 50-60 nm. The HCV genome is a single-stranded, positive-sense RNA of about 9,600 bp coding for a polyprotein of 3009-3030 amino-acids, which is cleaved co and post-translationally by cellular and two viral proteinases 30 into mature viral proteins (core, E1, E2, p7, NS2, NS3, NS4A, NS4B, NS5A, NS5B). It is believed that the structural proteins, E1 and E2, the major glycoproteins are embedded into a viral lipid envelope and form stable heterodimers. It is also believed that the structural core protein interacts with the viral RNA genome to 35 form the nucleocapsid. The nonstructural proteins designated NS2 to NS5 include proteins with enzymatic functions involved in virus replication and protein processing including a polymerase, protease and helicase.

O The main source of contamination with HCV is blood. The magnitude

of the HCV infection as a health problem is illustrated by the prevalence among high-risk groups. For example, 60% to 90% of hemophiliacs and more than 80% of intravenous drug abusers in western countries are chronically infected with HCV. For intravenous drug abusers, the prevalence varies from about 28% to 70% depending on the population studied. The proportion of new HCV infections associated with post-transfusion has been markedly reduced lately due to advances in diagnostic tools used to screen blood donors.

10

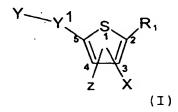
The only treatment currently available for HCV infection is interferon-α (IFN-α). However, according to different clinical studies, only 70% of treated patients normalize alanine aminotransferase (ALT) levels in the serum and after discontinuation of IFN, 35% to 45% of these responders relapse. In general, only 20% to 25% of patients have long-term responses to IFN. Clinical studies have shown that combination treatment with IFN and ribavirin (RIBA) results in a superior clinical response than IFN alone. Different genotypes of HCV respond differently to IFN therapy, genotype 1b is more resistant to IFN therapy than type 2 and 3.

There is therefore a great need for the development of anti-viral agents.

25

SUMMARY OF THE INVENTION

In one aspect, the present invention provides novel compounds represented by formula I:



30

or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$- \begin{matrix} N \\ N \\ R_3 \end{matrix} \qquad \text{or} \qquad \begin{matrix} R_2 \\ I \\ N \\ R_3 \end{matrix} \qquad ;$$

wherein,

٠5

M is chosen from:

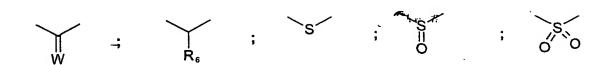
wherein,

R₄ is C ₁₋₆ alkyl;

 $\rm R_8$ is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ 10 aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and $\rm R_{15}$ is chosen from H or C $_{1-6}$ alkyl;

10

35



wherein W is chosen from O, S or NR,

wherein R₇ is chosen from H, C ₁₋₁₂ alkyl, C ₂₋₁₂ alkenyl, C₂₋₁₂ alkynyl, C ₆₋₁₄ aryl, C ₃₋₁₂ heterocycle, C₃₋₁₂ heteroaralkyl, C ₆₋₁₆ aralkyl;

and R_{6} is chosen from H, C $_{1-12}$ alkyl, C $_{6-14}$ aryl or C $_{6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{-2-6} alkenyl or C_{-2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_5$, $P(O)OR_aOR_b$, $S(O)OR_5$, $S(O)_2OR_5$, tetrazole, $CON(R_9)CH(R_5)COOR_5$, $CONR_{10}R_{11}$, $CON(R_9)-SO_2-R_5$, $CONR_9OH$ or halogen, wherein R_9 , R_5 , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 $\rm R_a$ and $\rm R_b$ are each independently chosen from H, C $_{1\text{--}12}$ alkyl, C $_{2\text{--}12}$ alkynyl, C $_{6\text{--}14}$ aryl, C $_{3\text{--}12}$ heterocycle, C $_{3\text{--}18}$

20 heteroaralkyl and C₆₋₁₈ aralkyl;

or R and R are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl; 25 provided that R_{16} is other than methyl or ethyl;

 R_1 is chosen from C $_{2-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl or C $_{6-18}$ aralkyl;

30 R_2 is chosen from C $_{2-12}$ alkyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl, or C $_{6-18}$ aralkyl;

R₃ is chosen from H, C $_{i-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-16}$ heteroaralkyl or C $_{6-18}$ aralkyl;

Z is chosen from H, halogen, C₁₋₆ alkyl;

WO 02/100851 with the proviso that:

10

35

PCT/CA02/00876

i) when X is 4-Chloro-2,6-dimethyl-benzenesulfonamide and, R₁ is phenyl, and R₃ is H, and Y¹ is a bond, then Y is other than CONH₂; compound #580

- ii) when X is Toluene-4-sulfonamide and R_1 is 4-chloro-phenyl, and R_3 is H, and Y¹ is a bond, then Y is other than CONH₂; compound #563
- iii) when X is Toluene-4-sulfonamide and R_1 is 4-fluoro-phenyl, and R_3 is H, and Y is a bond, then Y is other than $CONH_2$; compound #564
- 15 iv) when X is Toluene-4-sulfonamide and R_1 is 4-methoxy-phenyl, and R_3 is H, and Y¹ is a bond, then Y is other than $CONH_2$; compound #565
- v) when X is Benzamide and R_1 is phenyl Y is a bond and Y is 20 COOH then R is other than hydrogen.

The compounds of the present invention are useful in therapy, particularly as antivirals.

- In another aspect, there is provided a method of treating viral infections in a subject in need of such treatment comprising administering to the subject a therapeutically effective amount of a compound of formula (I) or composition of the invention.
- In still another aspect, there is provided a method of treating viral infections in a subject in need of such treatment comprising administering to the subject a combination comprising at least one compound of formula (I) and at least one further therapeutic agent.

In another aspect, there is provided a pharmaceutical formulation comprising the compound of the invention in combination with a pharmaceutically acceptable carrier or excipient.

Another aspect of the invention is the use of a compound according to formula (I), for the manufacture of a medicament for the treatment of viral infections.

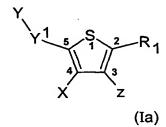
In another aspect, there is provided a method for inhibiting or reducing the activity of viral polymerase in a host comprising administering a therapeutically effective amount of a compound of formula (I).

10 DETAILED DESCRIPTION OF THE INVENTION

In one embodiment, compounds of the present invention comprise those wherein the following embodiments are present, either independently or in combination.

15

In one embodiment, the present invention provides novel compounds of formula (Ia):



or pharmaceutically acceptable salts thereof;

20

wherein,

X is chosen from:

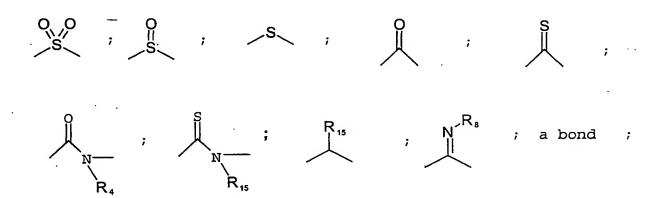
$$N_{R_1}^{M_1}$$
 or $N_{R_3}^{R_2}$;

WO 02/100851

PCT/CA02/00876

wherein,

M is chosen from:



5 wherein,

10

15

20

R₄ is C ₁₋₆ alkyl;

 R_8 is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R_{15} is chosen from H or C $_{1-6}$ alkyl;

J is chosen from:

wherein W is chosen from O, S or NR,

wherein R_7 is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl;

and R_6 is chosen from H, C $_{1-12}$ alkyl, C $_{6-14}$ aryl or C $_{6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(0)OR_{2}OR_{5}$, $S(0)OR_{5}$, $S(0)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-16} heteroaralkyl, C_{6-16} aralkyl;

or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

- or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;
- R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl and C $_{6-18}$ aralkyl; provided that R_{16} is other than methyl or ethyl;
- 10 R₁ is chosen from C $_{2-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl or C $_{6-18}$ aralkyl;
 - $\rm R_2$ is chosen from C $_{2-12}$ alkyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl, or C $_{6-18}$ aralkyl;
 - R_3 is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl or C $_{6-18}$ aralkyl;
 - Z is chosen from H, halogen, C₁₋₆ alkyl;

with the proviso that:

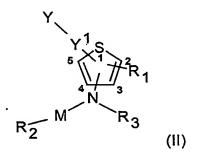
15

20

- i) when X is 4-Chloro-2,6-dimethyl-benzenesulfonamide and, R_1 is phenyl, and R_3 is H, and Y¹ is a bond, then Y is other than CONH₂; compound #580
 - ii) when X is Toluene-4-sulfonamide and R_1 is 4-chloro-phenyl, and R_3 is H, and Y¹ is a bond, then Y is other than $CONH_2$; compound #563
- iii) when X is Toluene-4-sulfonamide and R_1 is 4-fluoro-phenyl, and R_3 is H, and Y is a bond, then Y is other than $CONH_2$; compound #564
- 35 iv) when X is Toluene-4-sulfonamide and R_1 is 4-methoxy-phenyl, and R_3 is H, and Y¹ is a bond, then Y is other than $CONH_2$; compound #565

v) when X is Benzamide and R_1 is phenyl Y is a bond and Y is COOH then R_1 is other than hydrogen.

In a further aspect, the present invention provides novel compounds represented by formula II:

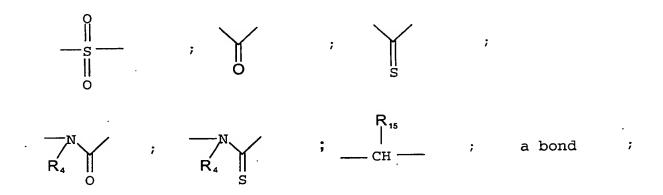


and pharmaceutically acceptable salts thereof,

wherein,

10

M is chosen from:



15 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $CO-COOR_{5}$, $PO_{3}R_{a}R_{b}$, $SO_{3}R_{5}$, tetrazole, $CON(R_{s})CH(R_{5})-COOR_{5}$, $CON(R_{10}R_{11})$ or $CONR_{5}OH$, wherein

each R_s R_9 , $R_{10},\ R_{11},\ R_{16},\ R_a,$ and R_b are independently chosen 20 from H or C $_{1-6}$ alkyl,;

 R_1 is chosen from C $_{1-6}$ alkyl, C $_{2-6}$ alkenyl,C $_{2-6}$ alkynyl, C $_{6-12}$ aryl, C $_{3-10}$ heterocycle, C_{3-10} heteroaralkyl, C $_{6-12}$ aralkyl, or a halogen;

WO 02/100851

PCT/CA02/00876

 R_2 is chosen from C $_{6-12}$ aryl, C $_{3-10}$ heterocycle, C $_{6-12}$ aralkyl or C_{3-10} heteroaralkyl;

 R_3 is chosen from H or C_{1-6} alkyl; C_{6-12} aralkyl or C_{3-10} beteroaralkyl;

 R_4 is chosen from H or C $_{1-6}$ alkyl; R_{15} is chosen from H or C $_{1-6}$ alkyl

- 10 with the proviso that:
 - i) when M is



and R_1 is 4-chloro-2,5-dimethyl-phenyl, R_1 is phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than CONH₂; compound #580

ii) when M is



15

and R_2 is 4-methylphenyl, R_1 is 4-chloro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than CONH₂; compound #563

20 iii) when M is



and R_2 is 4-methylphenyl, R_1 is 4-fluoro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than CONH₂; compound #564

25 iv) when M is

WO 02/100851

PCT/CA02/00876



and R_2 is 4-methylphenyl, R_1 is 4-methoxy-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than CONH₂; compound #565

In still a further embodiment, the present invention provides novel compounds of formula (IIa):

$$\begin{array}{c} Y \\ Y^{1} & S \\ & & \\ &$$

wherein,

M is chosen from:

10

Y' is chosen from a bond, C1-6 alkyl, C 2-6 alkenyl or C 2-6 alkynyl;

15 Y is chosen from $COOR_{16}$, $CO-COOR_{5}$, $PO_{3}R_{a}R_{b}$, $SO_{3}R_{5}$, tetrazole, $CON(R_{9})CH(R_{5})-COOR_{5}$, $CON\ R_{10}R_{11}$ or $CONR_{9}OH$, wherein each $R_{5}\ R_{9}$, R_{10} , R_{11} , R_{16} , R_{a} , and R_{b} are independently chosen from H or C $_{1-6}$ alkyl,;

 R_1 is chosen from C $_{1-6}$ alkyl, C $_{2-6}$ alkenyl, C $_{2-6}$ alkynyl, C $_{6-12}$ aryl, 20 C $_{3-10}$ heterocycle, C $_{3-10}$ heteroaralkyl, C $_{6-12}$ aralkyl, or a halogen;

 R_{2} is chosen from C $_{6-12}$ aryl, C $_{3-10}$ heterocycle, C $_{6-12}$ aralkyl or C_{3-10} heteroaralkyl;

5 R_3 is chosen from H or C_{1-6} alkyl; C_{6-12} aralkyl or C_{3-10} heteroaralkyl;

 R_4 is chosen from H or C $_{1-6}$ alkyl; R_{15} is chosen from H or C $_{1-6}$ alkyl;

10

with the proviso that:

i) when M is



and R_2 is 4-chloro-2,5-dimethyl-phenyl, R_1 is phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than CONH₂; compound #580

ii) when M is



and R_2 is 4-methylphenyl, R_1 is 4-chloro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than CONH₂; compound #563

20

iii) when M is



and R_2 is 4-methylphenyl, R_1 is 4-fluoro-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than CONH,; compound #564

25

iv) when M is



and R_2 is 4-methylphenyl, R_1 is 4-methoxy-phenyl, and R_3 is H, and Y^1 is a bond, then Y is other than CONH,; compound #565.

In one embodiment, X is:



In a further embodiment, X is:



In one embodiment, Z is chosen from H, halogen, C_{1-6} alkyl. In further embodiments,

10 Z is H

5

Z is halogen

Z is fluoride

Z is C₁₋₆ alkyl

Z is chosen from methyl, trifluoromethyl, ethyl, propyl,

isopropyl, cyclopropyl, butyl, isobutyl, cyclobutyl, pentyl, neopentyl, cyclopentyl, hexyl or cyclohexyl.

20 In further embodiments;

 R_1 is chosen from C_{2-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl.

 R_1 is chosen from a C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle.

 R_1 is a C_{2-12} alkyl.

25 R_1 is a C_{6-14} aryl.

 R_1 is a C_{3-12} heterocycle.

R₁ is chosen from t-butyl, isobutyl, allyl, ethynyl, 2-phenylethenyl, isobutenyl, benzyl, phenyl, phenethyl,

benzodioxolyl, thienyl, thiophenyl, pyridinyl, isoxazolyl, thiazolyl, pyrazolyl, tetrazolyl, benzofuranyl, indolyl, furanyl, or benzothiophenyl any of which can be optionally substituted by one or more substituent chosen from halogen,

- nitro, nitroso, SO_2R_{12} , PO_3RcRd , $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(0)C_{1-6}$ alkyl, $C(0)C_{2-6}$ alkenyl, $C(0)C_{2-6}$ alkynyl, $C(0)C_{6-12}$ aryl, $C(0)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(0)OR_{12}$, cyano, azido, amidino or guanido;
- wherein R₁₂, Rc, Rd, R₁₃ and R₁₄ are each independently chosen from H, C₁₋₁₂ alkyl, C₂₋₁₂ alkenyl, C₂₋₁₂ alkynyl, C₆₋₁₄ aryl, C₃₋₁₂ heterocycle, C₃₋₁₈ heteroaralkyl, C₆₋₁₈ aralkyl;
 - or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
- or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
 - R_1 is chosen from thienyl, t-butyl, phenyl or pyridinyl.
 - R_{i} is isoxazolyl substituted by at least one methyl.
 - R_1 is pyridinyl.

In one embodiment, R_1 is chosen from a C_{1-6} alkyl, C_{6-12} aryl or C_{3-10} heterocycle.

In one embodiment, R₁ is chosen from t-butyl, isobutyl, allyl,
25 ethynyl, 2-phenylethenyl, isobutenyl, benzyl, phenyl, phenethyl,
benzodioxolyl, thienyl, thiophenyl, pyridinyl, isoxazolyl,
thiazolyl, pyrazolyl, tetrazolyl, benzofuranyl, indolyl,
furanyl, or benzothiophenyl, any of which can be substituted by
at least one substituent chosen from C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆
30 alkynyl, C₃₋₁₀ heterocycle, halogen, nitro, CONR₁₃R₁₄, NR₁₃R₁₄,
amidino, guanido, Cyano, SO₂-C₁₋₆ alkyl, C(O)OR₁₂, C₁₋₆ alkyloxy, C₂₋₆
alkenyloxy, C₂₋₆ alkynyloxy, or C₆₋₁₂ aryloxy;
wherein R₁₂, R₁₃ and R₁₄ are each independently chosen from H, C₁₋₁₂
alkyl, C₂₋₁₂ alkenyl, C₂₋₁₂ alkynyl, C₆₋₁₄ aryl, C₃₋₁₂ heterocycle, C₃₋₁₈
heteroaralkyl, C₆₋₁₈ aralkyl;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

In one embodiment, R₁ is chosen from thienyl, t-butyl, phenyl, thiophenyl, pyridinyl, isoxazolyl, any of which can be substituted by at least one substituent chosen from a halogen, C₁₋₆ alkyl, C₁₋₆ alkyloxy, C₂₋₆ alkenyl, C₂₋₆ alkynyl, nitro, cyano, SO₂-C₁₋₆ alkyl, NO-C₁₋₆ alkyl.

- 10 In further embodiments;
 - R, is phenyl.
 - R, is phenyl substituted with fluoride.
 - R, is phenyl substituted with at least one fluoride
 - R, is phenyl di-substituted with fluoride.
- 15 R, is phenyl substituted with chloride.
 - R, is phenyl substituted with at least one chloride
 - R, is phenyl di-substituted with chloride.
 - R_1 is phenyl substituted with fluoride and chloride.
 - R, is phenyl substituted with nitro...
- 20 R, is phenyl substituted with at least one nitro.
 - R, is phenyl substituted with methoxy.
 - R, is phenyl substituted with OCF,.
 - R, is phenyl substituted with CF,.
 - R_1 is phenyl substituted with methyl.
- 25 R_1 is phenyl substituted with at least one methyl.
 - R, is phenyl substituted with CN.
 - R, is phenyl substituted with SO2-CH3.
 - R, is phenyl substituted with NH(CO)-CH,.
- 30 In further embodiments,
 - R, is thiophenyl.
 - R, is thiophenyl substituted by at least one halogen.
 - R, is thiophenyl substituted by at least one chloride.
 - R, is thiophenyl substituted by at least one methyl.
- 35 $R_{\rm i}$ is thiophenyl substituted by at least one methyl and one chloride.
 - In further embodiments,
 - R, is thienyl.

R, is thienyl substituted by at least one halogen.

R, is thienyl substituted by at least one chloride.

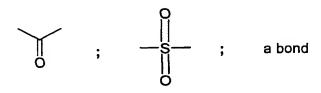
R, is thienyl substituted by at least one methyl.

 R_i is thienyl substituted by at least one methyl and one 5 chloride.

 R_{1} is isoxazole di-substituted with CH_{3} .

R, is pyridine.

In one embodiment, M is chosen from:



10

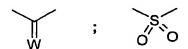
In a further embodiment, M is:



In an alternative embodiment, M is:



15 In one embodiment, J is chosen from:



wherein, W is as defined above.

In an alternative embodiment, J is:



20

In a further embodiment, J is:



In one embodiment, Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(0)OR_{2}OR_{5}$, $S(0)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CONR_{9}OH$.

In a further embodiment, any of R_5 , Ra, Rb, R_9 , R_{10} , R_{11} and R_{16} are each independently chosen from H or C_{1-6} alkyl; provided that R_{16} is other than methyl or ethyl.

In one embodiment, Y is chosen from $COOR_{16}$, $CONR_{10}R_{11}$ or $CON(R_{\bullet})CH(R_{5})-COOR_{5}$.

In a further embodiment, any of R_5 , R_9 , R_{10} , R_{11} and R_{16} are each independently chosen from H or C_{1-6} alkyl; provided that R_{16} is other than methyl or ethyl.

In a further embodiment, Y is chosen from $COOR_{16}$, $CONR_{10}R_{11}$ or $CONR_{10}R_{11}$

In a further embodiment, Y is chosen from $COOR_5$, $CONR_5R_5$ or $CON(R_5)CH(R_5)_COOR_5$.

In a further embodiment, Y is COOH.

In a further embodiment, Y is CONH₂.

20 In a further embodiment, Y is CONHCH, COOH.

In a further embodiment, Y is COOCH,.

In a further embodiment, Y^1 is chosen from CH_2 , C=CH, $CH-CH_2$ or a bond.

25

In further embodiments;

 R_3 is chosen from H, C_{1-12} alkyl, C_{6-18} aralkyl, C_{3-12} heterocycle or C_{3-18} heteroaralkyl.

 $\rm R_{\rm 3}$ is chosen from H, $\rm C_{\rm 1-12}\,alkyl,\,C_{\rm 6-18}\,aralkyl$ or $\rm C_{\rm 3-12}\,heterocycle.$

30 R_3 is C_{1-12} alkyl.

R, is C₆₋₁₈ aralkyl.

 R_3 is C_{3-12} heterocycle.

R, is chosen from H, methyl, ethyl, i-propyl, cyclopropyl, cyclohexyl, allyl, piperidinyl, piperazinyl, pyrrolidinyl, azetidinyl, aziridinyl, pyridinyl, piperidinylmethyl, dioxanyl, dioxolanyI, azepanyl or benzyl; any of which can be optionally 5 substituted by one or more substituent chosen from halogen, nitro, nitroso, SO_3R_{12} , PO_3RcRd , $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(0)C_{1-6}$ alkyl, $C(0)C_{2-6}$ alkenyl, $C(0)C_{2-6}$ alkynyl, $C(0)C_{6-12}$ aryl, $C(0)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, 10 NR₁₃R₁₄, C(0)OR₁₂, cyano, azido, amidino or guanido; wherein R₁₂, Rc, Rd, R₁₃ and R₁₄ are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C₃₋₁₈ heteroaralkyl, C₆₋₁₈ aralkyl; or Rc and Rd are taken together with the oxygens to form a 5 to 15 10 membered heterocycle; or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

 R_3 is chosen from H or Methyl, isopropyl, piperidinyl, piperidinylmethyl, dioxolanyl or cyclohexyl.

20

In a further embodiment, R₃ is H or methyl.
In a further embodiment, R₃ is H.
In a further embodiment, R₃ is methyl.
In a further embodiment, R₃ is benzyl, thiophenylmethyl,
furanylmethyl.

In additional embodiments; R_2 is C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle; R_2 is C_{3-6} heterocycle.

- 30 R₂ is chosen from thienyl, furanyl, pyridinyl, oxazolyl, thiazolyl, pyrrolyl, benzofuranyl, indolyl, benzoxazolyl, benzothienyl, benzothiazolyl, piperazinyl, pyrrolidinyl or quinolinyl any of which can be optionally substituted by one or more substituent chosen from halogen, nitro, nitroso, SO₃R₁₂,
- 35 PO_3RCRd , $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{4-12} aralkyl, C_{4-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{4-12} aryloxy,

 $C(0)C_{1-6}$ alkyl, $C(0)C_{2-6}$ alkenyl, $C(0)C_{2-6}$ alkynyl, $C(0)C_{6-12}$ aryl,

- $C(0)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(0)OR_{12}$, cyano, azido, amidino or guanido;
- wherein R_{12} , Rc, Rd, R_{13} and R_{14} are each independently chosen from
- 5 H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
 - or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
 - or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to
 - R, is a heterocycle chosen from thienyl, furanyl, pyridinyl, pyrrolyl, indolyl, piperazinyl or benzothienyl.
 - R_2 is C_{2-12} alkyl.

10 10 membered heterocycle.

- R, is chosen from cyclopropyl, cyclobutyl, cyclopentyl,
- oyclopentenyl cyclohexyl, cycloheptyl, 2-(cyclopentyl)-ethyl, methyl, ethyl, vinyl, propyl, propenyl, isopropyl, butyl, butenyl isobutyl, pentyl, neopentyl or t-butyl any of which can be optionally substituted by one or more substituent chosen from halogen, nitro, nitroso, SO₃R₁₂, PO₃RcRd, CONR₁₃R₁₄, C₁₋₆ alkyl, C₂₋₆
- alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(0)C_{1-6}$ alkyl, $C(0)C_{2-6}$ alkenyl, $C(0)C_{2-6}$ alkynyl, $C(0)C_{6-12}$ aryl, $C(0)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, NR13R14, $C(0)OR_{12}$, cyano, azido, amidino or guanido;
- wherein R_{12} , Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-13} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
 - or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
- 30 or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
 - R_2 is C_{6-12} aryl.
 - R, is an aryl chosen from indenyl, naphthyl or biphenyl.

 R_2 is phenyl substituted by one or more substituent chosen from halogen, nitro, nitroso, SO_3R_{12} , PO_3RcRd , $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(0)C_{1-6}$ alkyl, $C(0)C_{2-6}$

- 5 alkenyl, C(0)C₂₋₆ alkynyl, C(0)C₆₋₁₂ aryl, C(0)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, NR₁₃R₁₄, C(0)OR₁₂, cyano, azido, amidino or guanido;
 - wherein R_{12} , Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle,
- 10 C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
 - or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
 - or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
- 15 R₂ is phenyl substituted by one or two substituents chosen from halogen, nitro, nitroso, SO₃R₁₂, PO₃RcRd, CONR₁₃R₁₄, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, C₆₋₁₂ aryloxy, C(0)C₁₋₆ alkyl, C(0)C₂₋₆ alkenyl, C(0)C₂₋₆ alkynyl, C(0)C₆₋₁₂ aryl, C(0)C₆₋₁₂ aralkyl, C₃₋₁₀
- 20 heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(0)OR_{12}$, cyano, azido, amidino or guanido;
 - wherein R_{12} , Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
- or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
 - or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
- R₂ is phenyl substituted by one or more substituent chosen from halogen, nitro, CONR₁₃R₁₄, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆ alkyloxy, C(O)C₁₋₆ alkyl, C₆₋₁₂ aryl, C₃₋₁₀ heterocycle, hydroxyl, NR₁₃R₁₄, C(O)OR₁₂, cyano, azido, wherein R₁₂, R₁₃ and R₁₄ are each independently chosen from H, C₁₋₁₂ alkyl, C₂₋₁₂ alkenyl, C₂₋₁₂ alkynyl, C₆₋₁₄ aryl, C₃₋₁₂ heterocycle, C₃₋₁₈ heteroaralkyl, C₆₋₁₈ aralkyl;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

- R_2 is phenyl substituted by one or two substituents chosen from halogen, nitro, $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} alkyloxy,
- 5 C(O)C₁₋₆ alkyl, C₆₋₁₂ aryl, C₃₋₁₀ heterocycle, hydroxyl, NR₁₃R₁₄, C(O)OR₁₂, cyano, azido, wherein R₁₂, R₁₃ and R₁₄ are each independently chosen from H, C₁₋₁₂ alkyl, C₂₋₁₂ alkenyl, C₂₋₁₂ alkynyl, C₆₋₁₄ aryl, C₃₋₁₂ heterocycle, C₃₋₁₈ heteroaralkyl, C₆₋₁₈ aralkyl; or R₁₃ and R₁₄ are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
 - R_2 is phenyl substituted by one or two substituents chosen from halogen, C_{1-6} alkyl, $NR_{13}R_{14}$, nitro, $CONR_{13}R_{14}$, $C(0)OC_{1-6}$ alkyl, COOH or C_{1-6} alkyloxy $C(0)OR_{12}$, cyano, azido, wherein R_{12} , R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12}
- 15 alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
 - or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
- In one embodiment, R_2 is chosen from C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, 20 C $_{6-12}$ aralkyl or C_{3-10} heteroaralkyl.
 - In a further embodiment, R_2 is chosen from a C_{6-12} aryl or C_{3-10} heterocycle.
 - In a further embodiment, R_2 is a C_6 aryl or a C_{3-6} heterocycle. In a further embodiment, R_2 is chosen from phenyl, pyridinyl,
- thiophenyl, benzofuran, thiazole, pyrazole, substituted with at least one substituent chosen from a halogen, C₁₋₆ alkyl, C₁₋₆ alkyloxy, CF₃, COOH, COOC₁₋₆ alkyl, cyano, NH₂, nitro, NH(C₁₋₆ alkyl), N(C₁₋₆ alkyl)₂ or a C₃₋₈ heterocycle.
- R₂ is chosen from thienyl, furanyl, pyridyl, oxazolyl, thiazolyl, pyrrolyl, benzofuranyl, indolyl, benzoxazolyl, benzothienyl, benzothiazolyl or quinolinyl any of which can be substituted by at least one substituent chosen from C₁₋₆ alkyl, amino, halogen, nitro, amido, CN, COOC₁₋₆ alkyl, or C₁₋₆ alkyloxy.
 - R, is methylphenyl.
- 35 R, is dichlorophenyl.

In a further embodiment, R, is chosen from:

wherein:

5

Rw is H, O or methyl;

Ry is H or methyl;

Rw is H;

Rw is methyl;

10 Ry is H;

Ry is methyl;

and wherein, Xa is S, N, O or carbon.

In a further embodiment, each of Ra, Rb, Rc, Rd, Re, and Rf are
independently chosen from, H, Cl, Br, I, F, C₁₋₆ alkyl, OC₁₋₆

5 alkyl, CF₃, COOH, COOC₁₋₆ alkyl, CN, NH₂, NO₂, NH(C₁₋₆ alkyl), N(C₁₋₆ alkyl)₂.

In a further embodiment, each of Ra, Rb, Rc, Rd, Re, and Rf are
independently chosen from, H, Cl, Br, I, F, methyl, O-methyl,
10 CF3, COOH, COOCH3, CN, NH2, NO2, NH(CH3) or N(CH3)2.

In a further embodiment, each of Ra, Rb, Rc, Rd, Re, and Rf are independently chosen from, H, Cl, Br, I, F, methyl, O-methyl, CF_3 , COOH, COOCH₃, CN, NH_2 , or NO_2 .

In a further embodiment, each of Ra, Rb, Rc, Rd, Re, and Rf are independently chosen from, H, Cl, methyl, O-methyl, CF_3 , COOH, $COOCH_3$, CN, NH_2 , or NO_2 .

20 In a further embodiment, each of Ra, Rb, Rc, Rd, Re, and Rf are independently chosen from, H, Cl, F, methyl, CF3 or O-methyl.

In one embodiment, Rf is H or methyl.

In another embodiment, Rf is H.

25 In another embodiment, Rf is methyl.

In a further embodiment, each of Ra, Rb, Rc, Rd and Re is independently chosen from, H or Cl.

In a further embodiment, each of Ra, Rb, Rc, Rd and Re is H.

30 In one embodiment:

Ra is chosen from Cl, F, methyl or O-methyl;

Rb is H;

15

Rc is chosen from Cl, F, methyl or O-methyl;

Rd is H;

35 Re is chosen from Cl, F, methyl or O-methyl.

In one embodiment:

Ra is methyl;

Rb is H; -

5 Rc is Cl;

Rd is H;

Re is methyl.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, Br, I, F, C₁₋₆ alkyl, OC₁₋₆ alkyl, CF₃, COOH, COOC₁₋₆ alkyl, CN, NH₂, NO₂, NH(C₁₋₆ alkyl), N(C₁₋₆ alkyl)₂.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, Br, I, F, methyl, O-methyl, CF₃, COOH,

COOCH₃, CN, NH₂, NO₂, NH(CH₃) or N(CH₃)₂.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, Br, I, F, methyl, O-methyl, CF_3 , COOH, $COOCH_3$, CN, NH_2 , or NO_2 .

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, Br, I, F, methyl, O-methyl, CF3, COOH, COOCH3, CN, NH2, or NO2.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, methyl, O-methyl, CF_3 , COOH, COOCH₃, CN, NH_2 , or NO_2 .

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H, Cl, F, methyl, CF_3 or O-methyl.

In a further embodiment, each of Rs, Rt, Ru, are independently chosen from, H or Cl.

35 In a further embodiment, each of Rs, Rt, Ru, are H.

In one embodiment:

Rs and Ru are Cl and Rt is H.

Rs is Cl, Rt and Ru are H.

5

In one embodiment, the viral infection is chosen from Flavivirus infections.

In one embodiment, the Flavivirus infection is chosen from

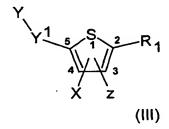
Hepatitis C virus (HCV), bovine viral diarrhea virus (BVDV), hog

cholera virus and yellow fever virus.

In another embodiment, the Flavivirus infection is Hepatitis C viral infection.

15

In one embodiment, there is provided a method for treating or preventing a Flaviviridae viral infection in a host comprising administering to the host a therapeutically effective amount of at least one compound of formula (III)



20

or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N$$
 R_2
or
 N
 R_3
 R_3

25

wherein,

M is chosen from:

$$R_{4}$$
, R_{15} , R_{15

wherein,

R, is chosen from H or C 1-6 alkyl;

5 R_s is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R_{15} is chosen from H or C $_{1-6}$ alkyl;

J is chosen from:

wherein

10

W is chosen from O, S or NR,

wherein R_7 is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-12}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl;

and $\rm R_{6}$ is chosen from H, C $_{\rm 1-12}$ alkyl, C $_{\rm 6-12}$ aryl or C $_{\rm 6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

- Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{a}OR_{b}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{9})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{9})-SO_{2}-R_{5}$, $CONR_{9}OH$ or halogen, wherein R_{9} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;
- or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

- or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;
 - R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;
- R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl, or halogen;
 - R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;
- 15 R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;
 - Z is chosen from H, halogen, C₁₋₆ alkyl.
- In one embodiment, there is provided a method for treating or preventing Flaviviridae viral infection in a host comprising administering to the host a therapeutically effective amount of at least one compound of formula (III), further comprising at least one antiviral agent.

25

- In one embodiment, the antiviral agent is chosen from a viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor.
- 30 In a further embodiment, the antiviral agent is chosen from interferon α and ribavirin.
 - In a further embodiment, said compound of formula (III) and said antiviral agent are administered sequentially.

35

In a further embodiment, said compound of formula (III) and said antiviral agent are administered simultaneously.

In one embodiment, there is provided a method for treating or preventing Flaviviridae viral infection in a host comprising administering to the host a therapeutically effective amount of at least one compound of formula (III) and at least one additional agent chosen from immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.

In another embodiment, the additional agent is chosen from silybum marianum, interleukine-12; amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

In further embodiments;

The compound of formula (III) and the additional agent are administered sequentially.

15 The compound of formula (III) and the additional agent are administered simultaneously.

In one embodiment, the present invention further provides A pharmaceutical composition comprising at least one compound having the formula III or pharmaceutically acceptable salts thereof; and at least one pharmaceutically acceptable carrier or excipient.

In a further embodiment, the pharmaceutical composition, is 25 further comprising one or more additional agent chosen from antiviral agent, immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.

In one embodiment, the antiviral agent is chosen from a viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor.

In one embodiment, the antiviral agent is chosen from interferon α and ribavirin.

In one embodiment, the additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N35 acetyl cysteine or cyclosporin.

In one embodiment, the invention further provides the use of a compound having the formula III for the manufacture of a medicament for treating or preventing a viral Flaviridea infection in a host

5

In one embodiment, there is provided the use of a compound having the formula III or pharmaceutically acceptable salts thereof in therapy

In one embodiment, the invention provides the use of a compound having the formula III for treating or preventing Flaviviridae viral infection in a host.

In one embodiment, the use of a compound having the compound of formula III for treating or preventing Flaviviridae viral

infection in a host is further comprising one or more additional agent chosen from antiviral agent, immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.

In one embodiment, the antiviral agent is chosen from a viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor.

In one embodiment, the antiviral agent is chosen from interferon $\boldsymbol{\alpha}$ and ribavirin.

In one embodiment, the additional agent is chosen from silybum 25 marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

In one embodiment, the compound of formula III and the additionnal agent are administered sequentially.

In one embodiment, the compound of formula III and the 30 additionnal agent are administered simultaneously.

In one embodiment, there is provided a method for inhibiting or reducing the activity of viral polymerase in a host comprising administering a therapeutically effective amount of a compound of formula (III).

In one embodiment, the method for inhibiting or reducing the activity of viral polymerase in a host comprising administering a therapeutically effective amount of a compound of formula (III) is further comprising one or more viral polymerase

In further embodiments;

5 inhibitor.

The viral polymerase is a Flaviviridae viral polymerase. The viral polymerase is a RNA-dependant RNA-polymerase.

The viral polymerase is HCV polymerase.

10

In one embodiment, the invention provides a method for inhibiting or reducing the activity of viral helicase in a host comprising administering a therapeutically effective amount of a compound having the formula III.

15

In one embodiment, the invention provides a method for inhibiting or reducing the activity of viral helicase in a host comprising administering a therapeutically effective amount of a compound chosen from:

- Compound #14 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-chloro-phenyl)-thiophene-2-carboxylic acid
- Compound #19 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid
- Compound #223 3-(4-Bromo-2-fluorobenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid
- Compound #224 3-(4-Bromo-2-methylbenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid
- Compound #225 5-(4-Isobutylphenyl 3-(3-methoxy-benzenesulfonyl-amino)-thiophene-2-carboxylic acid
- Compound #581 5-(4-Isobutyl-phenyl)-3-[5-(5-trifluoromethyl-isoxazol-3-yl)-thiophene-2-sulfonylamino]-thiophene-.

 2-carboxylic acid
- Compound #227 3-[2,5-Bis-(2,2,2-trifluoroethoxy)
 benzenesulfonylamino]-5-(4-isobutyl-phenyl)
 thiophene-2-carboxylic acid
- Compound #228 3-(2-Chloro-4-cyanobenzenesulfonylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid

Compound #582 5-(4-Isobutyl-phenyl)-3-(2,3,4-trifluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid or pharmaceutically acceptable salts thereof.

In further embodiments;

The viral helicase is a flaviviridea helicase.

The viral helicase is HCV helicase.

5

In a further embodiment, there is provided the use of a compound having the formula III for inhibiting or reducing the activity of viral polymerase in a host.

10 In still a further embodiment, there is provided the use of a compound having the formula III for inhibiting or reducing the activity of viral polymerase in a host, further comprising one or more viral polymerase inhibitor.

In further embodiments;

The viral polymerase is Flaviviridae viral polymerase.

The viral polymerase is RNA-dependant RNA-polymerase.

The viral polymerase is HCV polymerase.

In one embodiment, the invention provides the use of a compound 20 having the formula III for inhibiting or reducing the activity of viral helicase in a host.

In one embodiment, the invention provides the use of a compound chosen from:

- Compound #14 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-chloro-phenyl)-thiophene-2-carboxylic acid
- Compound #19 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid
- Compound #223 3-(4-Bromo-2-fluorobenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid
- Compound #224 3-(4-Bromo-2-methylbenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid
- Compound #225 5-(4-Isobutylphenyl 3-(3-methoxy-benzenesulfonyl-

WO 02/100851 PCT/CA02/00876 amino)-thiophene-2-carboxylic acid

Compound #581 5-(4-Isobutyl-phenyl)-3-[5-(5-trifluoromethyl-isoxazol-3-yl)-thiophene-2-sulfonylamino]-thiophene-2-carboxylic acid

- Compound #227 3-[2,5-Bis-(2,2,2-trifluoroethoxy)
 benzenesulfonylamino]-5-(4-isobutyl-phenyl)
 thiophene-2-carboxylic acid
- Compound #228 3-(2-Chloro-4-cyanobenzenesulfonylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid
- Compound #582 5-(4-Isobutyl-phenyl)-3-(2,3,4-trifluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid or pharmaceutically acceptable salts thereof for inhibiting or reducing the activity of viral helicase in a host.

In one embodiment, the invention provides the use of a compound having the formula III for inhibiting or reducing the activity of viral helicase in a host further comprising one or more viral helicase inhibitor.

In further embodiments;

10 The viral helicase is Flaviviridae viral helicase.

The viral helicase is HCV helicase.

In one embodiment, the present invention provides a combination comprising a compound having the formula III and one or more additionnal agent chosen from viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor, immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.

In a further embodiment, the additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine, cyclosporin, interferon α and ribavirin.

In further embodiments;

The compound of formula (III) and the additionnal agent are administered sequentially.

The compound of formula (III) and the additionnal agent are administered simultaneously.

5

In still a further embodiment, the present invention provides_a process for preparing a compound of formula A:

10 said process comprising the steps of adding:

- an enol ether;
- an hydride donating agent; and
- an organic carboxylic acid;

15

to a compound of formula B:

wherein;

20

Y is chosen from a bond, C₁₋₆ alkyl, C 2-6 alkenyl or C 2-6 alkynyl;

Y is chosen from COOR₁₆, COCOOR₅, P(O)OR₂OR₅, S(O)OR₅, S(O)₂OR₅, tetrazole, $CON(R_s)CH(R_s)COOR_s$, $CONR_{10}R_{11}$, $CON(R_s)-SO_2-R_s$, $CONR_sOH$ or 25 halogen, wherein $R_{\rm s},\ R_{\rm s},\ R_{\rm lo}$ and $R_{\rm ll}$ are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl; or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

- or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;
 - R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;
- R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl or halogen;
 - R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;
- 15 R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;
 - Z is chosen from H, halogen, C1-6 alkyl.
- It will be appreciated by those skilled in the art that the compounds of formula (I) or (Ia) can contain a chiral centre on the general formula (I). The compounds of formula (I) or (Ia) thus exist in the form of two different optical isomers (i.e. (+) or (-) enantiomers). All such enantiomers and mixtures thereof including racemic mixtures are included within the scope of the invention. The single optical isomer or enantiomer can be obtained by method well known in the art, such as chiral HPLC, enzymatic resolution and chiral auxiliary.
- 30 In accordance with the present invention, the compounds of formula (I) or (Ia) include:
 - Compound 1 3-[(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-(3-IODO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
- 35
 Compound 2 3-[(3-BENZOFURAN-2-YL-BENZYL)-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
- Compound 3 3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-40 THIOPHENE-2-CARBOXYLIC ACID
 - Compound 4 3-{(2,4-DICHLORO-BENZOYL)-[5-(3-TRIFLUOROMETHYL-PHENYL)-FURAN-2-YLMETHYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

	Compound	5	3-[(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	6	5-(4-FLUORO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	7	3-(2,4-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	8	3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	9	3-[(2,4-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	10	5- TERT -BUTYL-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	11	4-(TOLUENE-4-SULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID
25	Compound	12	3-[(5-BENZOFURAN-2-YL-THIOPHEN-2-YLMETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHÉNYL-THIOPHENE-2-CARBOXYLIC ACID
23	Compound	13	5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	14	3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-CHLORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	15	5-PHENYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	16	5-PHENYL-3-(TOLUENE-3-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	17	3-BENZENESULFONYLAMINO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	18	3-(4-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID
45	Compound	19	3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
43	Compound	20	5-TERT-BUTYL-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
50	Compound	21	3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	22	3-(4-METHOXY-2,3,6-TRIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	23 `	5-PHENYL-3-(THIOPHENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	24	4-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)- [2,3']BITHIOPHENYL-5-CARBOXYLIC ACID
60	Compound	25	5-(3,5-BIS-TRIFLUOROMETHYL-PHENYL)-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

			-
	WO 02/100851		PCT/CA02/00876
	Compound	26	8-CHLORO-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-4H- 1,5-DITHIA-CYCLOPENTA[A]NAPHTHALENE-2-CARBOXYLIC ACID
5	Compound	27	3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	28	3-[3-(2,6-DICHLORO-PYRIDIN-4-YL)-UREIDO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	29	3-(2-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	30	3-(2-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	31	5-PHENYL-3-(2-TRIFLUOROMETHOXY-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	32	3-(4- TERT -BUTYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	33	3-(4-CHLORO-PHENOXYCARBONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	34	3-(3,4-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	35	5-PHENYL-3-(2-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	36	3-(5-BROMO-6-CHLORO-PYRIDINE-3-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	37	3-(5-CHLORO-THIOPHENE-2-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound .	38	3-(5-CHLORO-3-METHYL-BENZO[B]THIOPHENE-2-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	39	3-(4-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	40	3-(3-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	41	3-(5-CHLORO-1,3-DIMETHYL-1H-PYRAZOLE-4-SULFONYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	42	3-(3-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	43	3-(4-ISOPROPYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	44	3-(2,6-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	45	3-(2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	46	5-PHENYL-3-(5-[1,2,3]THIADIAZOL-4-YL-THIOPHENE-2-

SULFONYLAMINO) -THIOPHENE-2-CARBOXYLIC ACID

	WO 02/10	0851	PCT/CA02/00876	
	Compound	47	5-PHENYL-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIACID	:C
5	Compound	48	3-(2,4-DICHLORO-BENZYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLI ACID	:C .
	Compound	49	3-(3-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
10	Compound	50	5-PHENYL-3-(3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHE 2-CARBOXYLIC ACID	NE-
15	Compound	51	3-(2-CARBOXY-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID METHYL ESTER	
15	Compound	52	5-PHENYL-3-(4-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-THIOPHE 2-CARBOXYLIC ACID	:NE-
·20	Compound	53	3-(2,5-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
	Compound .	54	3-(2-CYANO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
25	Compound	55	3-(2,5-DICHLORO-THIOPHENE-3-SULFONYLAMINO)-5-PHENYL-THIOPHE 2-CARBOXYLIC ACID	NE-
30	Compound	56	4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	: ·
30	Compound	57	5'-CHLORO-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	•
35	Compound	58	5-(2,4-DICHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHE 2-CARBOXYLIC ACID	NE-
	Compound	59	5-(4-NITRO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	-
40	Compound	60	3-(TOLUENE-2-SULFONYLAMINO)-5-(4-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	
45	Compound	61	5-QUINOLIN-8-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	
43	Compound	62	5-PHENYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	3
50	Compound	63	5-(3-NITRO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	•
	Compound	64	3-(TOLUENE-2-SULFONYLAMINO)-5-M-TOLYL-THIOPHENE-2-CARBOXYLIACID	C
55	Compound	65	5-(3-CHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2 CARBOXYLIC ACID	}-
60	Compound	66	5-(4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2 CARBOXYLIC ACID	}-
U	Compound	67	5-(3-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2 CARBOXYLIC ACID	}-·

			•
	WO 02/100851		PCT/CA02/00876
	Compound	68	5-(4-CHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	69	5-(3,5-DIFLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	70	5-(3,4-DIFLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	71	3-(TOLUENE-2-SULFONYLAMINO)-5-VINYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	72	3-(4-CHLORO-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	73	3-[(4-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	74	5-PHENYL-3-[(THIOPHENE-2-CARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	75	3-[METHYL-(THIOPHENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	76	3-(2-BROMO-BENZENESULFONYLAMINO)~5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	77	3-(2,4-DIFLUORO-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	78	3-[(2,4-DIFLUORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	79	3-(TOLUENE-2-SULFONYLAMINO)-5-TRIMETHYLSILANYLETHYNYL-THIOPHENE-2-CARBOXYLIC ACID
33	Compound	80	5-ETHYNYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC
40	Compound	81	3-(TOLUENE-2-SULFONYLAMINO)-5-(3-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	. 82	5-BENZOYL-3-(TOLUENE-2-SULFONYLAMÍNO)-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	83	5-(4-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	84	5-(3-CHLORO-4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	85	5-(3,4-DICHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	86	5-PYRIDIN-4-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	87	5-PYRIDIN-3-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	88	3-(TOLUENE-2-SULFONYLAMINO)-5-(4-TRIFLUOROMETHYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID

	WO 02/10	0851	PCT/CA02/00876
	Compound	89	5-(4-METHANESULFONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	90	5-(3-ACETYLAMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	91	5-(3-CHLORO-4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	92	3-(4-METHYL-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound.	93	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	94	3-(3,5-DIMETHYL-ISOXAZOLE-4-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	95	3-[(2-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	96	3-(2-METHYL-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	97	3-[METHYL-(2-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
23	Compound	98	5-PHENYL-3-(5-TRIFLUOROMETHYL-PYRIDINE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
30	Compound	99	5-PHENYLETHYNYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	100	3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	101	5-(2-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
. 40	Compound	102	5-(2-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
.0	Compound	103	5-(2-ETHOXYCARBONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
45	Compound	104	5-(2-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	105	3'-METHYL-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5- CARBOXYLIC ACID
50	Compound	106	3-(TOLUENE-2-SULFONYLAMINO)-5-(2-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	107	3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
33	Compound ACID	108	5-STYRYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC
60	Compound	109	3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-(4-NITRO-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID
	Compound	110	3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

			•
•	Compound	111	3-[[5-(3-CHLORO-4-FLUORO-PHENYL)-THIOPHEN-2-YLMETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	112 —	3-[(4-OXO-1-PHENYL-1,3,8-TRIAZA-SPIRO[4.5]DECANE-8-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	113	3-{[4-(2-0X0-2,3-DIHYDRO-BENZOIMIDAZOL-1-YL)-PIPERIDINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	114	3-{[4-(4-NITRO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	115	5-(2-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	116	5-(4-CHLORO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	117	5-(3-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	118	3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID
23	Compound	119	3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	120	5-PHENETHYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	121	5-(3-ETHOXYCARBONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
35	Compound	122	5-(4-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	123	5-(3-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	124	5-(4'-BROMO-BIPHENYL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
45	Compound	125	5-(4-HYDROXYMETHYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	126	5-FURAN-3-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	127	5-BENZOFURAN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	128	5-PYRIDIN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	129	5-(4-NITRO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	130	3-[(BENZOFURAN-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	131	3-[(2,4-DIMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

	Compound .	132	3-[[5-(2-CYANO-PHENYL)-THIOPHEN-2-YLMETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	133 —	5-(4-FLUORO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	134	5-[2-(4-CHLORO-PHENYL)-VINYL]-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	135	3-BENZENESULFONYLAMINO-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	136	3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	137	5-PHENYL-3-(2-VINYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	138	3-(4-BROMO-2,5-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25`	Compound	139	3-(2-ACETYLAMINO-4-METHYL-THIAZOLE-5-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
23	Compound	140	3-(4-ACETYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	141	3-(4-FLUORO-2-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	142	3-(2-METHOXY-4-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	143	3-(3,4-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	144	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-5-(4-CHLORO-PHENYL)-2-METHYL-FURAN-3-CARBOXYLIC ACID ETHYL ESTER
.0	Compound	145	3-(4-FLUORO-3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	146	3-(2-AMINO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	147	3-(3-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	148	3-(4-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	149	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
33	Compound	150	5-(3-CYANO-BENZYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	151	5-PHENYL-3-(2,4,6-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	152	3-(4-METHOXY-2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

	Compound	153	5-PHENYL-3-(2,3,4-TRICHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	154 —	5-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2-METHYL-FURAN-3-CARBOXYLIC ACID METHYL ESTER
	Compound	155	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2-METHYL-1,5-DIPHENYL-1H-PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER
10	Compound.	156	5-PHENYL-3-{[4-(3-TRIFLUOROMETHYL-PHENYL)-PIPERAZINE-1-CARBONYL]-AMIN}-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	157	3-{{4-(4-FLUORO-PHENYL)-PIPERAZINE-1-CARBONYL}-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	158	3-{[4-(2,6-DIMETHYL-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	159	3-{[4-(2-CHLORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	160	3-{[4-(3-CHLORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	161	4,4'-BIS-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5,5'-DICARBOXYLIC ACID
30	Compound	162	3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	163	5-(1-DIMETHYLSULFAMOYL-1H-PYRAZOL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	164	5-(3-AMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	165	5-(4-AMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	166	5-(4-ACETYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	167	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2,5-DIMETHYL-1H-PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER
	Compound	168	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-5-(4-CHLORO-PHENYL)-3-METHYL-1-PHENYL-1H-PYRROLE-2-CARBOXYLIC ACID ETHYL ESTER
50	Compound	169	•
55	Compound	170	
,,,	Compound	171	
60	Compound	172	•

WO 02/100851 PCT/CA02/00876 3-{[2-(4-FLUORO-PHENYL)-ACETYL]-METHYL-AMINO}-5-PHENYL-Compound 173 THIOPHENE-2-CARBOXYLIC ACID 3-(4-PENTYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-174 Compound 5 CARBOXYLIC ACID Compound 175 3-(METHYL-PHENYLACETYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACTD 10 176 3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)-BENZENESULFONYLAMINO]-5-Compound PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-(4-METHYL-2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-Compound 2-CARBOXYLIC ACID 15 Compound 178 5-THIAZOL-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID 5-PHENYL-3-[3-(3-PHENYL-PROPYL)-UREIDO]-THIOPHENE-2-CARBOXYLIC Compound 179 20 180 3-[(3,4-DIHYDRO-1H-ISOQUINOLINE-2-CARBONYL)-AMINO]-5-PHENYL-Compound THIOPHENE-2-CARBOXYLIC ACID 25 Compound 181 3-{[4-(4-METHOXY-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-{[4-(6-METHYL-PYRIDIN-2-YL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-Compound 182 PHENYL-THIOPHENE-2-CARBOXYLIC ACID HYDROCHLORIDE 30 3-{[4-(4-CHLORO-BENZYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-Compound PHENYL-THIOPHENE-2-CARBOXYLIC ACID HYDROCHLORIDE 5-(5-METHYL-PYRIDIN-2-YL)-3-(TOLUENE-2-SULFONYLAMINO)-Compound 184 35 THIOPHENE-2-CARBOXYLIC ACID 3-[ETHYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-185 Compound CARBOXYLIC ACID 3-[(3-CHLORO-THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-40 186 Compound THIOPHENE-2-CARBOXYLIC ACID Compound 187 3-[(2-BROMO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 45 188 3-[(4-BUTYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-Compound CARBOXYLIC ACID 3-(2-CHLOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-189 Compound 50 CARBOXYLIC ACID 5-(4-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-Compound 190 CARBOXYLIC ACID 5-(5-CHLORO-PYRIDIN-2-YL)-3-(TOLUENE-2-SULFONYLAMINO)-55 191 Compound THIOPHENE-2-CARBOXYLIC ACID 5-(4-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-Compound 192 THIOPHENE-2-CARBOXYLIC ACID 60 Compound 193 5-(4-CYANO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-

THIOPHENE-2-CARBOXYLIC ACID

			- ·	
	WO 02/10	0851	PCT/CA02/00876	
	Compound	194	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-NITRO-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	
5	Compound	195	5-(4-HYDROXYMETHYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	
	Compound	196	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-NITRO-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	
10	Compound	197	5-(4-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	
	Compound	198	5-(4-METHOXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	
15	Compound	199	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	
20	Compound	200	5-(4-AMINO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	
	Compound	201	3-[CYCLOPENTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
25	Compound	202	5-BENZO[1,3]DIOXOL-5-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHEN 2-CARBOXYLIC ACID	E-
•	Compound	203	3-[(2-HYDROXY-ETHYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
30	Compound	204	3-[(2,4-DICHLORO-BENZOYL)-ISOBUTYL-AMINO]-5-PHENYL-THIOPHENE 2-CARBOXYLIC ACID	;-
35	Compound	205	3-[(2-METHOXY-4-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
	Compound	2.06	5-(3-CYANO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	
40	Compound	207	5-(2-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	
45	Compound	208	3-[(2,4-DICHLORO-BENZOYL)-PHENYL-AMINO]-5-PHENYL-THIOPHENE-2 CARBOXYLIC ACID	-
43	Compound	209	3-[4-(TRIFLUOROMETHYL-BENZOYL)METHYLAMINE]-5-PHENYL-THIOPHEN 2-CARBOXYLIC ACID	Œ~
50	Compound	210	3-[(4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	•
	Compound	211	3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	-
55	Compound	212	5-(3,5-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	•
60	Compound	213	5-(3-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	
00	Compound	214	5-(2,4-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	-

	WO 02/10	0851	PCT/CA02/00876
	Compound	215	5-(4-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
5	Compound	216	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	217	5-(2-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	218	3-[(2-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	219	3-[(3,5-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	220	3-(4-BROMO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	221	3-(5-CARBOXY-4-CHLORO-2-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	222	5-PHENYL-3-(2,3,4-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	223	3-(4-BROMO-2-FLUORO-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	224	3-(4-BROMO-2-METHYL-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	225	5-(4-ISOBUTYL-PHENYL)-3-(3-METHOXY-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
35	Compound	226	3-[(4-FLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
•	Compound	227	3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)-BENZENESULFONYLAMINO]-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	228	3-(2-CHLORO-4-CYANO-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
4.5	Compound	229	5'-ACETYL-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
45	Compound	230	5-BENZO[B]THIOPHEN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	231	5-(4-BUTYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	232	5-(4-ETHYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	233	3-[BENZYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	234	3-[(4-CHLORO-2-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
ου	Compound	235	3-[(2,4-DIMETHYL-BENZENESULFONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

			1
	WO 02/10	0851	PCT/CA02/00876
	Compound	236	5-(4-ACETYL-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	237	5-(4-ACETYL-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	238	5-(4-ACETYL-PHENYL)-3-(4-CHLORO-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
10	Compound	239	5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID TERT-BUTYL ESTER
	Compound	240	3-[(2,4-DIMETHYL-BENZENESULFONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	241	3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	242	3-ETHANESULFONYLAMINO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	243	3-[ISOPROPYL-(4-TRIFLUOROMETHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	244	3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL-BUT-2-ENYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	245	3-[(2,6-DICHLORO-PYRIDINE-3-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	246	3-[(6-CHLORO-PYRIDINE-3-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	247	3-[(4-TERT-BUTYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
33	Compound	248	5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	249	5-(4-ETHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	250	3-[(2,6-DICHLORO-PYRIDINE-3-CARBONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	251	3-[(BENZO[B]THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	252	3-[METHYL-(NAPHTHALENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	253	3-[(3,4-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	254 _.	3-[(3,5-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	255	3-[(4-BROMO-3-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	256	3-[(3-CHLORO-BENZO[B]THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID

	WO 02/10	0051	DCT/C 4.02/00976
	WO 02/10	257	PCT/CA02/00876 3-[METHYL-(4-METHYL-3-NITRO-BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
5	Compound	258	5-(4-CARBAMOYL-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	259	5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	260	5-(1H-INDOL-5-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
1.5	Compound	261	3-[SEC -BUTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	262	3-[(2,4-DIMETHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound .	263	5-(4-AZIDO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	264	3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
25	Compound	265	5-(4-CARBAMOYL-PHENYL)-3-(4-CHLORO-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
30	Compound	266	5-(2-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
30	Compound	267	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5- O -TOLYL-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	268	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-M-TOLYL-THIOPHENE-2- CARBOXYLIC ACID
	Compound	269	5-(3-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
40	Compound	270	5-(3,4-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	271	5-(3-AMINO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
	Compound	272	5-(3-ACETYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
50	Compound	273	5-(3-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
	Compound	274	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	275	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	276	3-[(3,4-DIMETHOXY-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	277	3-[METHYL-(2,4,6-TRIFLUORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID

	WO 02/100851 Compound 278		PCT/CA02/00876	
			3-[(2,3-DIFLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
5	Compound	279	3-[(3-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
	Compound	280	3-[(2,3-DIFLUORO-4-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
10	Compound	281	3-[(2-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
15	Compound	282	5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	
13	Compound	283	5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	
20	Compound	284	3-[(2-BROMO-4-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
	Compound	285	3-(2,6-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
25	Compound	286	3-[METHYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
30	Compound	287	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE 2-CARBOXYLIC ACID METHYL ESTER	:-
	Compound	288	5-(4-CYANO-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	
35	Compound	289	3-(4-CHLORO-BENZENESULFONYLAMINO)-5-(4-CYANO-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	
	Compound	290	5-(4-CYANO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	
40	Compound	291	5'-ACETYL-4-(2,4-DIMETHYL-BENZENESULFONYLAMINO)- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	
45	Compound	292	5'-ACETYL-4-(2,6-DIMETHYL-BENZENESULFONYLAMINO)- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	
	Compound	293	3-[METHYL-(4-METHYL-THIOPHENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
50	Compound	294	5-(3-CHLORO-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	
	Compound	295	5'-CYANO-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	
55	Compound	296	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PYRIDIN-2-YL-THIOPHENE-2-CARBOXYLIC ACID	•
60	Compound	297	3-[(2,4-DICHLORO-THIOBENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
00	Compound	298	5-PHENYL-3-(2,4,6-TRIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2 CARBOXYLIC ACID	2-

	WO 02/100851		PCT/CA02/00876	
	Compound	299	3-[(1-CARBOXY-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
5	Compound	300	3-[(4-METHYL-BENZOYL)-(3-METHYL-BUT-2-ENYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
	Compound	301	3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
10	Compound	302	-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PYRIDIN-3-YL-THIOPHENE- 2-CARBOXYLIC ACID	
15	Compound	303	5'-ACETYL-4-[METHYL-(4-METHYL-BENZOYL)-AMINO]- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	
13	Compound	304	3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	
20	Compound	305	3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	
	Compound	306	3-[(2-BROMO-4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
25	Compound	307	3-[(4-CHLORO-2-FLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
30	Compound	308	3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-4-METHYL-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
50	Compound	309	3-[(2-BROMO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
35	Compound	310	3-[(4-CHLORO-2-IODO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
	Compound	311	3-['(4-CYANO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
40	Compound	312	3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-[4-(2-CARBOXY-VINYL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID	
45	Compound	313	3-[(4-CHLORO-2-HYDROXY-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
73	Compound	314	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-4-METHYL-5-PHENYL THIOPHENE-2-CARBOXYLIC ACID	
50	Compound	315	5- TERT -BUTYL-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	
	Compound	316	3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
55	Compound	317	3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
60	Compound	318	5-[4-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4-METHYL-BENZOYL)-PROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	
	Cómpound	319	5-BENZOFURAN-2-YL-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	

	WO 02/100851		PCT/CA02/00876
	Compound	320	3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-HYDROXYMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	321	3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-METHANESULFONYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
	Compound	322	5-[4-(2-CARBOXY-VINYL)-PHENYL]-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	323	3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-[3-(2-CARBOXY-VINYL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	324	3-[ISOPROPYL-(2,4,6-TRIMETHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
1.5	Compound	325	5-[3-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4-METHYL-BENZOYL)-PROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	326	3-[(2-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	327	3-[TERT -BUTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	328	3-[(2-AMINO-4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	329	3-[(4-CHLORO-2-NITRO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	. 330	3-[(4-METHYL-BENZOYL)-(3-TRIFLUOROMETHYL-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	331	3-[(3-FLUORO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	332	5-(4-CARBOXY-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	333	3-[CYCLOPROPYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	334	3-[(3-TERT-BUTYL-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
43	Compound	335	3-[(3-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	336	3-[(2,4-DIFLUORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	337	3-[(4-CHLORO-2,5-DIFLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	338	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(2-METHYL-ALLYL) THIOPHENE-2-CARBOXYLIC ACID
60	Compound	339	3-{ALLYL-[2-(4-CHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
υU	Compound	340	3-[BENZYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID

			
	WO 02/100851		PCT/CA02/00876
	Compound	341	3-[(4-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	342	3-[(4-METHYL-BENZOYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
•	Compound	343	3-[(4-METHYL-BENZOYL)-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	344	3-[(3-METHOXY-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
1.5	Compound	345	3-[(2-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	346	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-ISOBUTYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	347	3-[ALLYL-(2-NAPHTHALEN-2-YL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	348	3-{ALLYL-[2-(2,4-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	349	3-{ALLYL-[2-(2-CHLORO-4-FLUORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	350	3-{ALLYL-[2-(3,4-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	351	3-{ALLYL-[2-(2,4-DIFLUORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	352	3-{ALLYL-[2-(4-TRIFLUOROMETHYL-PHENYL)-ACETYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	353	3-{ALLYL-[2-(2,6-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
40	Compound .	354	3-[ALLYL-(2-M-TOLYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	355	5-(4-ACETYL-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
43	Compound	356	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	357	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	358	5'-ACETYL-4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
55	Compound	359	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(3- TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	360	4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5'-METHYL- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
55	Compound	361	3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-METHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

WO 02/100851 PCT/CA02/00876 Compound 362 3-(CYCLOHEXANECARBONYL-ISOPROPYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID Compound 363 3-{(2,4-DICHLORO-BENZOYL)-[1-(2,4-DICHLORO-BENZOYL)-PIPERIDIN-5 4-YL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 364 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-BENZOYL)-Compound AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT -BUTYL ESTER 10 Compound 365 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT -BUTYL ESTER 3-[(4-METHYL-BENZOYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-Compound 366 THIOPHENE-2-CARBOXYLIC ACID 15 367 5'-ACETYL-4-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-Compound [2,3']BITHIOPHENYL-5-CARBOXYLIC ACID 368 3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-Compound 20 THIOPHENE-2-CARBOXYLIC ACID Compound 369 5-(4-METHANESULFONYLAMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID 25 3-(4-FLUORO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-Compound 370 2-CARBOXYLIC ACID Compound 3-[(3-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-371 THIOPHENE-2-CARBOXYLIC ACID 30 3-(4-CHLORO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-372 Compound 2-CARBOXYLIC ACID Compound 373 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-METHANESULFONYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID 35 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-Compound 374 METHANESULFINYL-PHENYL) -THIOPHENE-2-CARBOXYLIC ACID 5-(4-CARBOXY-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-40 375 Compound AMINO]-THIOPHENE-2-CARBOXYLIC ACID 376 5-BENZOFURAN-2-YL-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-Compound THIOPHENE-2-CARBOXYLIC ACID 45 3-[(2-ACETOXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-Compound 377 THIOPHENE-2-CARBOXYLIC ACID 3-[ISOPROPYL-(2-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-Compound 378 50 THIOPHENE-2-CARBOXYLIC ACID 3-[ISOPROPYL-(2-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-Compound 379 THIOPHENE-2-CARBOXYLIC ACID 3-(CYCLOHEPTANECARBONYL-ISOPROPYL-AMINO)-5-PHENYL-THIOPHENE-2-55 Compound 380 CARBOXYLIC ACID Compound 381 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID 60 382 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-METHYL-THIOPHENE-Compound

2-CARBOXYLIC ACID

			·-
	WO 02/100851 Compound 383.		PCT/CA02/00876 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(3-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	384	3-[(3-CYCLOPENTYL-PROPIONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
	Compound 386 3-		3-(BUTYRYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-(METHYL-PENT-4-ENOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	387	3-[ISOPROPYL-(5-METHYL-3-OXO-3H-ISOINDOL-1-YL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	388	3-[METHYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	389	3-(METHYL-PENTANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	390	3-[METHYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	391	3-(CYCLOPENTANECARBONYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	392	3-[(3-CYCLOPENTYL-PROPIONYL)-ETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	393	3-(CYCLOBUTANECARBONYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	394	3-(BUT-2-ENOYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	395	3-[ISOPROPYL-(4-METHYL-2-VINYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	396	3-[ISOPROPYL-(4-METHYL-CYCLOHEX-1-ENECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	397	3-(ALLYL-HEXANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
4.5	Compound	398	3-(ALLYL-CYCLOBUTANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	399	3-(ALLYL-PENTANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	400	3-[ALLYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	401	3-[ALLYL-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	402	3-[(2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	403	3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	404	3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID

	WO 02/100851		-	PCT/CA02/00876
	Compound	405	3-[ISOPROPYL-(3-METHYL-CYCLOPENT-3-ENECAR PHENYL-THIOPHENE-2-CARBOXYLIC ACID	BONYL)-AMINO]-5-
5	Compound	406	3-[(2-BENZYLOXY-4-METHYL-BENZOYL)-ISOPROP TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBO	
	Compound	407	3-[(2,4-DIMETHYL-CYCLOHEXANECARBONYL)-ISO PHENYL-THIOPHENE-2-CARBOXYLIC ACID	PROPYL-AMINO]-5-
10	Compound	408	3-[ISOPROPYL-(3-METHYL-CYCLOPENTANECARBON THIOPHENE-2-CARBOXYLIC ACID	YL)-AMINO]-5-PHENYL-
	Compound	409	3-[(2-HYDROXY-4-METHYL-CYCLOHEXANECARBONY 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	L)-ISOPROPYL-AMINO]-
15	Compound	410	5-PHENYL-3-[PROPIONYL-(4-TRIFLUOROMETHYL-THIOPHENE-2-CARBOXYLIC ACID	BENZYL)-AMINO]-
20	Compound	411	3-[ISOBUTYRYL-(4-TRIFLUOROMETHYL-BENZYL)-THIOPHENE-2-CARBOXYLIC ACID	AMINO]-5-PHENYL-
	Compound	412	3-[(3-METHYL-BUTYRYL)-(4-TRIFLUOROMETHYL- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	BENZYL)-AMINO]-5-
25	Compound	413	3-[CYCLOPROPANECARBONYL-(4-TRIFLUOROMETHY PHENYL-THIOPHENE-2-CARBOXYLIC ACID	L-BENZYL)-AMINO]-5-
20	Compound	414	3-[CYCLOBUTANECARBONYL-(4-TRIFLUOROMETHYL PHENYL-THIOPHENE-2-CARBOXYLIC ACID	-BENZYL)-AMINO]-5-
30	Compound	415	3-[BUTYRYL-(4-TRIFLUOROMETHYL-BENZYL)-AMITHIOPHENE-2-CARBOXYLIC ACID	NO]-5-PHENYL-
35	Compound	416	3-[(2-CYCLOPENTYL-ACETYL)-(4-TRIFLUOROMET PHENYL-THIOPHENE-2-CARBOXYLIC ACID	THYL-BENZYL)-AMINO]-5
	Compound	417	3-[(4-TERT-BUTYL-BENZYL)-PROPIONYL-AMINO] 2-CARBOXYLIC ACID	-5-PHENYL-THIOPHENE-
40	Compound	418	3-[(4-NITRO-BENZYL)-PROPIONYL-AMINO]-5-PF CARBOXYLIC ACID	HENYL-THIOPHENE-2-
45	Compound	419	3-[(3-METHYL-BUTYRYL)-(4-NITRO-BENZYL)-ANTHIOPHENE-2-CARBOXYLIC ACID	INO]-5-PHENYL-
43	Compound	420	3-[CYCLOPROPANECARBONYL-(4-NITRO-BENZYL)-THIOPHENE-2-CARBOXYLIC ACID	-AMINO]-5-PHENYL-
50	Compound	421	3-[(2-CHLORO-BENZYL)-ISOBUTYRYL-AMINO]-5- CARBOXYLIC ACID	-PHENYL-THIOPHENE-2-
	Compound	422	3-[(2-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-FTHIOPHENE-2-CARBOXYLIC ACID	AMINO]-5-PHENYL-
55	Compound	423	3-[(2-CHLORO-BENZYL)-CYCLOPROPANECARBONYI THIOPHENE-2-CARBOXYLIC ACID	L-AMINO)-5-PHENYL-
60	Compound	424	3-[(ADAMANTANE-1-CARBONYL)-ISOPROPYL-AMINTHIOPHENE-2-CARBOXYLIC ACID	NO]-5-PHENYL-
UU	Compound	425	3-[(2-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-THIOPHENE-2-CARBOXYLIC ACID	-AMINO]-5-PHENYL-

			- man
	WO 02/100851		PCT/CA02/00876
	Compound	426	3-[ACETYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	427	3-[(2-METHYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	428	3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
10	Compound .	429	3-[(1-ACETYL-PIPERIDIN-4-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	430	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-[4-(1 H - TETRAZOL-5-YL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	431	3-[(2-CYANO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	432	3-[CYCLOBUTANECARBONYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	433	3-[BUTYRYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	434	3-[ACETYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	435	3-[CYCLOBUTANECARBONYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	436	3-[CYCLOHEXANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	437	3-[(4-TERT-BUTYL-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	438	3-[(4-TERT-BUTYL-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	439	3-[(4-TERT-BUTYL-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	440	3-[(4-TERT-BUTYL-BENZYL)-BUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	441	3-[(4-TERT-BUTYL-BENZYL)-CYCLOHEXANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	442	3-[(4-TERT-BUTYL-BENZYL)-(2-CYCLOPENTYL-ACETYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	443	3-[(2-CYCLOPENTYL-ACETYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
55	Compound	444	3-[(2-CHLORO-BENZYL)-CYCLOHEXANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	445	3-[(2-CYCLOPENTYL-ACETYL)-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	446	3-[BUTYRYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

WO 02/100851 PCT/CA02/00876 Compound 447 3-[BUTYRYL-(2-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 448 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5- M -Compound 5 TOLYL-THIOPHENE-2-CARBOXYLIC ACID 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-THIAZOL-2-YL-Compound 449 THIOPHENE-2-CARBOXYLIC ACID 10 Compound 450 3-(ACETYL-BENZYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID Compound 451 3-(BENZYL-PROPIONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-[BENZYL-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-15 452 Compound CARBOXYLIC ACID Compound 453 3-[BENZYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 20 454 3-(BENZYL-CYCLOPROPANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-Compound CARBOXYLIC ACID 3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-Compound 455 25 CARBOXYLIC ACID 3-[(4-CHLORO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-456 Compound CARBOXYLIC ACID 3-[(4-CHLORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-30 457 Compound CARBOXYLIC ACID 3-[(4-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-Compound 458 THIOPHENE-2-CARBOXYLIC ACID 35 3-[(4-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-Compound 459 THIOPHENE-2-CARBOXYLIC ACID 5-(4-ACETYL-PHENYL)-3-[ISOPROPYL-(4-METHYL-Compound 460 CYCLOHEXANECARBONYL) -AMINO] -THIOPHENE-2-CARBOXYLIC ACID . 40 3-[(4-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-Compound 461 THIOPHENE-2-CARBOXYLIC ACID 3-[BUTYRYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-45 Compound 462 CARBOXYLIC ACID 463. 3-[(4-CHLORO-BENZYL)-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-Compound THIOPHENE-2-CARBOXYLIC ACID 50 3-[ACETYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-Compound 464 THIOPHENE-2-CARBOXYLIC ACID 465 3-[ISOBUTYRYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-Compound 55 CARBOXYLIC ACID 466 3-[CYCLOPROPANECARBONYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-Compound THIOPHENE-2-CARBOXYLIC ACID 60 Compound 467 3-[(4-METHYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-

CARBOXYLIC ACID

	WO 02/100	0851	PCT/CA02/00876
	Compound	468	3-[ISOBUTYRYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
5	Compound	469	3-[CYCLOPROPANECARBONYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
•	Compound	470	3-[BUTYRYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
10	Compound	471	3-[(3-METHOXY-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	472	3-[(3-METHOXY-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound	473	3-[CYCLOBUTANECARBONYL-(3-METHOXY-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	474	3-[(2-CARBAMOYL-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	475	3-[BUTYRYL-(3-METHOXY-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	476	3-[ACETYL-(3-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	477	3-[(3-CHLORO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	478	3-[(3-CHLORO-BENZYL)-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
35	Compound	479	3-[(3-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
	Compound	480	3-[(3-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	481	3-[(3-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	482	3-[BUTYRYL-(3-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	483	3-[ACETYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
50	Compound	484	3-[(2,4-DIFLUORO-BENZYL)-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	485	3-[(2,4-DIFLUORO-BENZYL)-ISOBUTYRYL-AMINO}-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
55	Compound	486	3-[(2,4-DIFLUORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
60	Compound	487	3-[BENZYL-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
ου	Compound	488	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(1H-INDOL-5-YL)-THIOPHENE-2-CARBOXYLIC ACID

	WO 02/100	0851	PCT/CA02/00876	
	Compound	489	3-(BENZYL-CYCLOBUTANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
5	Compound	490	3-[CYCLOHEXANECARBONYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
	Compound	491	3-{ALLYL-[2-(4-METHOXY-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
10	Compound	492	3-(ETHYL-HEXANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
	Compound	493	3-(BUTYRYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
15	Compound	494	3-[ETHYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
	Compound	495	3-[CYCLOBUTANECARBONYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
20	Compound	496	3-[BUTYRYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
25	Compound	497	3-(CYCLOPENTANECARBONYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
25	Compound	498	3-(CYCLOHEXANECARBONYL-METHYL-AMINO)~5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
30	Compound	499	3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PYRROLIDINE-1-CARBOXYLIC ACID TERT-BUTYL ESTER	
	Compound	500	3-[(1,4-DIMETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
35	Compound	501	5-(4-ETHYL-PHENYL)-3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	
40	Compound	502	3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5- M -TOLYL-THIOPHENE-2-CARBOXYLIC ACID	
40	Compound	503	3-[(2,4-DICHLORO-BENZOYL)-PYRROLIDIN-3-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
45	Compound	504	4-{5-CARBOXY-4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO-2H-PYRIDINE-1-CARBOXYLIC ACID BENZYL ESTER	
50	Compound	505	3-{[2-(HYDROXYIMINO-METHYL)-4-METHYL-BENZOYL]-ISOPROPYL-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
30	Compound	506	3-[(1-CARBAMIMIDOYL-PIPERIDIN-4-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
55	Compound	507	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-AZEPANE-1-CARBOXYLIC ACID TERT -BUTYL ESTER	
	Compound	508	4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL) AMINO]-METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER	-
60	Compound	509	3-[AZEPAN-4-YL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	

	WO 02/100851		•	PCT/CA02/00876
	Compound	510	3-[(4-METHYL-CYCLOHEXANECARBONYL)-PIPERII PHENYL-THIOPHENE-2-CARBOXYLIC ACID LITHIU	DIN-4-YL-AMINO]-5- UM SALT
5	Compound	511	3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2 AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERM	,4-DICHLORO-BENZOYL)- r -Butyl ester
	Compound	512	3-[(4-BENZYLOXYCARBONYLAMINO-CYCLOHEXYL)- BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARI	
10	Compound	513	3-[ISOPROPYL-(4-METHYL-2-OXO-CYCLOHEXANEO PHENYL-THIOPHENE-2-CARBOXYLIC ACID	CARBONYL) -AMINO]-5-
15	Compound	514	3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-3-YL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITNEUTRAL COMPONENT	
	Compound	515	3-[(4-BENZYLOXYCARBONYLAMINO-CYCLOHEXYL)- BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARI	• •
20	Compound	516	3-[(2-BENZYLOXY-1-METHYL-ETHYL)-(2,4-DICE 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	HLORO-BENZOYL)-AMINO]-
25	Compound	517	3-[(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-(4-METCYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THICACID	THYL- OPHENE-2-CARBOXYLIC
	Compound	518	3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-1-HYDROXY-1-HYDROXY-1-HYDROXY-1-HYDROXYLIC AC	
30	Compound	519	3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YLI PHENYL-THIOPHENE-2-CARBOXYLIC ACID	METHYL-AMINO]-5-
35	Compound	520	3-[(2-CHLORO-BENZOYL)-PIPERIDIN-4-YLMETH THIOPHENE-2-CARBOXYLIC ACID	YL-AMINO]-5-PHENYL-
23	Compound	521	3-[(4,6-DICHLORO-1H-INDOLE-2-CARBONYL)-I PHENYL-THIOPHENE-2-CARBOXYLIC ACID	SOPROPYL-AMINO]-5-
40	Compound	522	3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-1-M PHENYL-THIOPHENE-2-CARBOXYLIC ACID	ETHYL-ETHYL)-AMINO]-5-
45	Compound	523	4-{1-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL) BENZOYL)-AMINO]-ETHYL}-PIPERIDINE-1-CARB ESTER	-(2,4-DICHLORO- OXYLIC ACID BENZYL
43	Compound .	524	4-{5-CARBOXY-4-[ISOPROPYL-(4-METHYL-CYCLAMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO-2 H -PACID BENZYL ESTER	
50	Compound	525	3-[(4-METHYL-CYCLOHEXANECARBONYL)-PYRIDI PHENYL-THIOPHENE-2-CARBOXYLIC ACID	N-4-YL-AMINO]-5-
55	Compound	526	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMING THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITACID	
	Compound	527	3-[ISOPROPYL-(4-PROPYL-CYCLOHEXANECARBON THIOPHENE-2-CARBOXYLIC ACID	YL)-AMINO]-5-PHENYL-
60	Compound	528	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2 AMINO]-CYCLOHEXYL-AMMONIUM; TRIFLUORO-AC	

WO 02/100851 PCT/CA02/00876 Compound 529 3-[(2,4-DICHLORO-BENZOYL)-(1-PIPERIDIN-4-YL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID 5 3-[(CYCLOHEX-3-ENECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-530 Compound THIOPHENE-2-CARBOXYLIC ACID 3-[(4-ETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-Compound 531 THIOPHENE-2-CARBOXYLIC ACID 10 3-[(4-CHLORO-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-532 Compound THIOPHENE-2-CARBOXYLIC ACID 4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-Compound 533 AMINO]-3-METHYL-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER 15 Compound 534 3-[(2,4-DICHLORO-BENZOYL)-(2-METHOXY-CYCLOHEXYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-[(2,4-DICHLORO-BENZOYL)-(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-20 535 Compound AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(1-536 Compound METHYL-PIPERIDIN-4-YL)-THIOPHENE-2-CARBOXYLIC ACID 25 3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL-PIPERIDIN-4-YL)-AMINO]-5-Compound 537 PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID 3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-CYCLOHEXYL)-AMINO]-5-30 538 Compound PHENYL-THIOPHENE-2-CARBOXYLIC ACID 4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYLCYCLOHEXANE Compound 539 CARBONYL)-AMINO]-METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL 35 ESTER ' 3-[((1R,2S,4R)-2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-Compound 540 ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-(ISOPROPYL-[1-(4-METHOXY-2,3,6-TRIMETHYL-BENZENESULFONYL)-5-40 541 Compound METHYL-1,2,3,6-TETRAHYDRO-PYRIDINE-2-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-4-FLUORO-5-PHENYL-Compound 542 45 THIOPHENE-2-CARBOXYLIC ACID 3-[(2,4-DICHLORO-BENZOYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-Compound 543 PHENYL-THIOPHENE-2-CARBOXYLIC ACID 4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYLCYCLOHEXANE 50 Compound 544 CARBONYL) - AMINO] - METHYL} - PIPERIDINIUM; TRIFLUORO - ACETATE 3-[(2-TERT-BUTOXYCARBONYLAMINO-1-METHYL-ETHYL)-(2,4-DICHLORO-545 Compound BENZOYL) -AMINO] -5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 55 2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-Compound 546 AMINO]-PROPYL-AMINE TRIFLUOROACETIC ACID SALT 3-[(3-CARBOXY-CYCLOPENTYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-Compound 547 60 PHENYL-THIOPHENE-2-CARBOXYLIC ACID 548 3-[(3-CARBOXY-CYCLOPENTYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-

PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound

	Compound	549	2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-
			AMINO]-CYCLOHEXYL-AMMONIUM CHLORIDE
5	Compound	550	3-(BENZOYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	551	{ [5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBONYL] - AMINO)-ACETIC ACID
10	Compound	552 :	5-BROMO-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
1.5	Compound .	553	3-[CYCLOHEXYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
15	Compound .	554	3-[[1,3]DIOXAN-5-YL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5 PHENYL-THIOPHENE-2-CARBOXYLIC ACID
20	Compound	555	3-[[2-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-1-METHYL-2-PHENYL-ETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
25	Compound	556	3-[[2-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-1-METHYL-2-PHENYL-ETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	557	3-[(2,4-DICHLORO-BENZOYL)-(2-DIETHYLAMINO-THIAZOL-5-YLMETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
30	Compound	558	(5-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-METHYL}-THIAZOL-2-YL)-DIETHYL-AMMONIUM; CHLORIDE
35	Compound	559	5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
	Compound	560	3-[((1S,2R,4S)-2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
40	Compound	561	3-[(2,4-DICHLORO-BENZOYL)-(2-METHOXY-1-METHYL-ETHYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
45	Compound	562	3-[(4S)-ISOPROPYL-(4-METHYL-CYCLOHEX-1-ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	566	3-METHYL-(4-METHYLBENZOYL)-AMINO)5-PHENYL THIOPHENE-2- CARBOXYLIC ACID (2-HYDROXY-ETHYL)AMIDE
50	Compound	567	5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID CYCLOBUTYLAMIDE
	Compound	568	3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID AMIDE
55	Compound	`569	5-BROMO-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
60	Compound	570	5-(4-CHLORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANE-CARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

WO 02/100851 PCT/CA02/00876 571 . 5-(4'-CHLORO-BIPHENYL-4-YL)-3-[ISOPROPYL-(4-METHYL-Compound CYCLOHEXANECARBONYL) - AMINO] - THIOPHENE - 2 - CARBOXYLIC ACID 572 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(TETRAHYDRO-PYRAN-4-YL)-Compound 5 AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 573 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-Compound AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 10 574 3-[(4-METHYL-CYCLOHEXANECARBONYL)-PIPERIDIN-4-YL-AMINO]-5-Compound PHENYL-THIOPHENE-2-CARBOXYLIC ACID Compound 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID 15 Compound 576 5-(4-CYANO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL) -AMINO] -THIOPHENE-2-CARBOXYLIC ACID 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(4-Compound METHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID 20 578 3-[(2-METHOXY-1-METHYL-ETHYL)-(4-METHYL-CYCLOHEXANECARBONYL)-Compound AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 579 3-[CYCLOHEXYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-25 Compound THIOPHENE-2-CARBOXYLIC ACID 581 5-(4-ISOBUTYL-PHENYL)-3-[5-(5-TRIFLUOROMETHYL-ISOXAZOL-3-YL)-Compound THIOPHENE-2-SULFONYLAMINO]-THIOPHENE-2-CARBOXYLIC ACID 30 Compound 582 5-(4-ISOBUTYL-PHENYL)-3-(2,3,4-TRIFLUORO-BENZENESULFONYLAMINO) -THIOPHENE-2-CARBOXYLIC ACID 3-[(2,4-DICHLORO-PHENYL)-ISOPROPYL-CARBAMOYL]-5-PHENYL-Compound 35 THIOPHENE-2-CARBOXYLIC ACID 3-(METHYL-P-TOLYL-CARBAMOYL)-5-PHENYL-THIOPHENE-2-CARBOXYLIC Compound ACID 585 3-[(2,4-DICHLORO-PHENYL)-METHYL-CARBAMOYL]-5-PHENYL-THIOPHENE-

or pharmaceutically acceptable salts thereof.

2-CARBOXYLIC ACID

Compound

40

50

45 Preferably, the compounds of the present invention are provided in the form of a single enantiomer at least 95%, more preferrably at least 97% and most preferably at least 99% free of the corresponding enantiomer.

More preferably the compound of the present invention are in the form of the (+) enantiomer at least 95% free of the corresponding (-) enantiomer.

More preferably the compound of the present invention are in the form of the (+) enantiomer at least 97% free of the corresponding (-) enantiomer.

More preferably the compound of the present invention are in the form of the (+) enantiomer at least 99% free of the corresponding (-) enantiomer.

In a more preferred embodiment, the compound of the present
invention are in the form of the (-) enantiomer at least 95%
free of the corresponding (+) enantiomer.

Most preferably the compound of the present invention are in the
form of the (-) enantiomer at least 97% free of the
corresponding (+) enantiomer.

15

More preferably the compound of the present invention are in the form of the (-) enantiomer at least 99% free of the corresponding (+) enantiomer.

- There is also provided a pharmaceutically acceptable salts of the present invention. By the term pharmaceutically acceptable salts of compounds of general formula (I) or (Ia) are meant those derived from pharmaceutically acceptable inorganic and organic acids and bases. Examples of suitable acids include hydrochloric, hydrobromic, sulphuric, nitric, perchloric, fumaric, maleic, phosphoric, glycollic, lactic, salicylic, succinic, toleune-p-sulphonic, tartaric, acetic, trifluoroacetic, citric, methanesulphonic, formic, benzoic, malonic, naphthalene-2-sulphonic and benzenesulphonic acids.

 Other acids such as oxalic, while not in themselves pharmaceutically acceptable, may be useful as intermediates in
- of ther acids such as oxalic, while not in themselves pharmaceutically acceptable, may be useful as intermediates in obtaining the compounds of the invention and their pharmaceutically acceptable acid addition salts.
- 35 Salts derived from appropriate bases include alkali metal (e.g. sodium), alkaline earth metal (e.g. magnesium), ammonium and NR₄+ (where R is C₁₋₄ alkyl) salts.

References hereinafter to a compound according to the invention includes compounds of the general formula (I)or (Ia) and their pharmaceutically acceptable salts.

- Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.
- 15 As used in this application, the term "alkyl" represents a straight chain, branched chain or cyclic hydrocarbon moiety which may optionally be substituted by one or more of: halogen, nitro, nitroso, SO3R12, PO3RcRd, CONR13R14, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C6-12 aralkyl, C6-12 aryl, C1-6 alkyloxy, C2-6
 20 alkenyloxy, C2-6 alkynyloxy, C6-12 aryloxy, C(0)C1-6 alkyl, C(0)C2-6 alkenyl, C(0)C2-6 alkynyl, C(0)C6-12 aryl, C(0)C6-12 aralkyl, C3-10 heterocycle, hydroxyl, NR13R14, C(0)OR12, cyano, azido, amidino or guanido;
- wherein R12, Rc, Rd, R13 and R14 are each independently chosen from H, C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C6-14 aryl, C3-12 heterocycle, C3-18 heteroaralkyl, C6-18 aralkyl; or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;

30

or R13 and R14 are taken together with the nitrogen to form a 3 to 10 membered heterocycle. Useful examples of alkyls include isopropyl, ethyl, fluorohexyl or cyclopropyl. The term alkyl is also meant to include alkyls in which one or more hydrogen atoms is replaced by an oxygen, (e.g. a benzoyl) or an halogen, more preferably, the halogen is fluoro (e.g. CF3- or CF3CH2-).

The terms "alkenyl" and "alkynyl" represent an alkyl containing at least one unsaturated group (e.g. allyl, acetylene,
40 'ethylene).

The term "aryl" represents a carbocyclic moiety containing at least one benzenoid-type ring which may optionally be substituted by one or more of halogen, nitro, nitroso, SO3R12, 5 PO3RcRd, CONR13R14, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C6-12 aralkyl, C6-12 aryl, C1-6 alkyloxy, C2-6 alkenyloxy, C2-6 alkynyloxy, C6-12 aryloxy, C(0)C1-6 alkyl, C(0)C2-6 alkenyl, C(0)C2-6 alkynyl, C(0)C6-12 aryl, C(0)C6-12 aralkyl, C3-10 heterocycle, hydroxyl, NR13R14, C(0)OR12, cyano, azido, amidino or guanido;

wherein R12, Rc, Rd, R13 and R14 are each independently chosen from H, C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C6-14 aryl, C3-12 heterocycle, C3-18 heteroaralkyl, C6-18 aralkyl;

or Rc and Rd are taken together with the oxygens to form a 5 to

10 membered heterocycle; or R13 and R14 are taken together with the nitrogen to form a 3 to 10 membered heterocycle. Examples of aryl include phenyl and

naphthyl.

20

The term "aralkyl" represents an aryl group attached to the adjacent atom by a C1-6alkyl, C1-6alkenyl, or C1-6alkynyl(e.g., benzyl).

The term "heterocycle" represents a saturated or unsaturated, cyclic moiety wherein said cyclic moeity is interrupted by at least one heteroatom, (e.g. oxygen, sulfur or nitrogen) which may optionally be substituted halogen, nitro, nitroso, SO3R12, PO3RcRd, CONR13R14, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C6-12 aralkyl, C6-12 aryl, C1-6 alkyloxy, C2-6 alkenyloxy, C2-6 alkynyloxy, C6-12 aryloxy, C(0)C1-6 alkyl, C(0)C2-6 alkenyl, C(0)C2-6 alkynyl, C(0)C6-12 aryl, C(0)C6-12 aralkyl, C3-10 heterocycle, hydroxyl, NR13R14, C(0)OR12, cyano, azido, amidino or guanido;

wherein R12, Rc, Rd, R13 and R14 are each independently chosen from H, C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C6-14 aryl, C3-12 heterocycle, C3-18 heteroaralkyl, C6-18 aralkyl; or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;

or R13 and R14 are taken together with the nitrogen to form a 3 to 10 membered heterocycle. It is understood that the term heterocyclic ring represents a mono or polycyclic (e.g., bicyclic) ring. Examples of heterocyclic rings include but are not limited to epoxide; furan; benzofuran; isobenzofuran; oxathiolane; dithiolane; dioxolane; pyrrole; pyrrolidine; imidazole; pyridine; pyrimidine; indole; piperidine; morpholine; thiophene and thiomorpholine.

10 The term "heteroaralkyl" represents an heterocycle group attached to the adjacent atom by a C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl.

When there is a sulfur atom present, the sulfur atom can be at different oxidation levels, ie. S, SO, or SO2. All such oxidation levels are within the scope of the present invention.

The term "independently" means that a substituent can be the same or different definition for each item.

20

As used in this application, the term "hydride donating agent "means a suitable ionic or covalent inorganic compound of hydrogen with another element (e.g. boron, sodium, lithium or aluminum) allowing the process to occur under the reaction conditions without causing adverse effect on the reagents or product. Useful examples of hydride donating agent include but are not limited to sodium borohydride (NaBH4), sodium cyanoborohydride (NaCNBH3), sodium triacetoxyborohydride (Na(OAc)3BH) and borane-pyridine complexe (BH3-Py).

30 Alternatively, resin or polymer supported hydride donating agent on a may be used.

The term "organic carboxylic acid" include but is not limited to aliphatic acid (e.g. acetic, formic, trifluoroacetic), aromatic acid (e.g. benzoic and salicylic), dicarboxylic acid (e.g. oxalic and phthalic). It will be apparent to one of ordinary skill that resin supported organic carboxylic acid may also be used.

The term "enol ether" as used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Enol ethers may be obtained commercially or prepared by well-known methods. Non-limiting examples of preparation include alkylation or silylation of enolates obtained from carbonyl compounds such as aldehydes, ketones, esters.

10 It will be appreciated that the amount of a compound of the invention required for use in treatment will vary not only with the particular compound selected but also with the route of administration, the nature of the condition for which treatment is required and the age and condition of the patient and will be ultimately at the discretion of the attendant physician or veterinarian. In general however a suitable dose will be in the range of from about 0.1 to about 750 mg/kg of body weight per day, preferably in the range of 0.5 to 60 mg/kg/day, most preferably in the range of 1 to 20 mg/kg/day.

20

The desired dose may conveniently be presented in a single dose or as divided dose administered at appropriate intervals, for example as two, three, four or more doses per day.

- 25 The compound is conveniently administered in unit dosage form; for example containing 10 to 1500 mg, conveniently 20 to 1000 mg, most conveniently 50 to 700 mg of active ingredient per unit dosage form.
- Ideally the active ingredient should be administered to achieve peak plasma concentrations of the active compound of from about 1 to about 75μM, preferably about 2 to 50 μM, most preferably about 3 to about 30 μM. This may be achieved, for example, by the intravenous injection of a 0.1 to 5% solution of the active ingredient, optionally in saline, or orally administered as a bolus containing about 1 to about 500 mg of the active ingredient. Desirable blood levels may be maintained by a continuous infusion to provide about 0.01 to about 5.0

mg/kg/hour or by intermittent infusions containing about 0.4 to about 15 mg/kg of the active ingredient.

While it is possible that, for use in therapy, a compound of the invention may be administered as the raw chemical it is preferable to present the active ingredient as a pharmaceutical formulation. The invention thus further provides a pharmaceutical formulation comprising compounds of formula (I) or (Ia) or a pharmaceutically acceptable derivative thereof together with one or more pharmaceutically acceptable carriers therefor and, optionally, other therapeutic and/or prophylactic ingredients. The carrier(s) must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

15

Pharmaceutical formulations include those suitable for oral, rectal, nasal, topical (including buccal and sub-lingual), transdermal, vaginal or parenteral (including intramuscular, sub-cutaneous and intravenous) administration or in a form

20 suitable for administration by inhalation or insufflation. The formulations may, where appropriate, be conveniently presented in discrete dosage units and may be prepared by any of the methods well known in the art of pharmacy. All methods include the step of bringing into association the active compound with liquid carriers or finely divided solid carriers or both and then, if necessary, shaping the product into the desired formulation.

Pharmaceutical formulation suitable for oral administration may
conveniently be presented as discrete units such as capsules,
cachets or tablets each containing a predetermined amount of the
active ingredient; as a powder or granules; as a solution, a
suspension or as an emulsion. The active ingredient may also be
presented as a bolus, electuary or paste. Tablets and capsules
for oral administration may contain conventional excipients such
as binding agents, fillers, lubricants, disintegrants, or
wetting agents. The tablets may be coated according to methods
well known in the art. Oral liquid preparations may be in the
form of, for example, aqueous or oily suspensions, solutions,
emulsions, syrups or elixirs, or may be presented as a dry

product for constitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, emulsifying agents, nonaqueous vehicles (which may include edible oils), or 5 preservatives.

The compounds according to the invention may also be formulated for parenteral administration (e.g. by injection, for example bolus injection or continuous infusion) and may be presented in unit dose form in ampoules, pre-filled syringes, small volume infusion or in multi-dose containers with an added preservative. The compositions may take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing an/or dispersing agents. Alternatively, the active ingredient may be in powder form, obtained by aseptic isolation of sterile solid or by lyophilisation from solution, for constitution with a suitable vehicle, e.g. sterile, pyrogen-free water, before use.

For topical administration to the epidermis, the compounds according to the invention may be formulated as ointments, creams or lotions, or as a transdermal patch. Such transdermal patches may contain penetration enhancers such as linalool, carvacrol, thymol, citral, menthol and t-anethole. Ointments and creams may, for example, be formulated with an aqueous or oily base with the addition of suitable thickening and/or gelling agents. Lotions may be formulated with an aqueous or oily base and will in general also contain one or more emulsifying agents, stabilizing agents, dispersing agents, suspending agents, thickening agents, or colouring agents.

Formulations suitable for topical administration in the mouth include lozenges comprising active ingredient in a flavoured base, usually sucrose and acacia or tragacanth; pastilles

35 comprising the active ingredient in an inert base such as gelatin and glycerin or sucrose and acacia; and mouthwashes comprising the active ingredient in a suitable liquid carrier.

Pharmaceutical formulations suitable for rectal administration 40 wherein the carrier is a solid are most preferably presented as

69

unit dose suppositories. Suitable carriers include cocoa butter and other materials commonly used in the art, and the suppositories may be conveniently formed by admixture of the active compound with the softened or melted carrier(s) followed by chilling and shaping in moulds.

Formulations suitable for vaginal administration may be presented as pessaries, tampons, creams, gels, pastes, foams or sprays containing in addition to the active ingredient such carriers as are known in the art to be appropriate.

For intra-nasal administration the compounds of the invention may be used as a liquid spray or dispersible powder or in the form of drops. Drops may be formulated with an aqueous or non-aqueous base also comprising one more dispersing agents, solubilising agents or suspending agents. Liquid sprays are conveniently delivered from pressurized packs.

For administration by inhalation the compounds according to the invention are conveniently delivered from an insufflator, nebulizer or a pressurized pack or other convenient means of delivering an aerosol spray. Pressurized packs may comprise a suitable propellant such as dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount.

Alternatively, for administration by inhalation or insufflation,
the compounds according to the invention may take the form of a
dry powder composition, for example a powder mix of the compound
and a suitable powder base such as lactose or starch. The
powder composition may be presented in unit dosage form in, for
example, capsules or cartridges or e.g. gelatin or blister packs
from which the powder may be administered with the aid of an
inhalator or insufflator.

When desired the above described formulations adapted to give sustained release of the active ingredient may be employed.

40

The compounds of the invention may also be used in combination with other antiviral agents or in combination with any additional agents useful in therapy and may be administered sequentially or simultaneously.

5

In one aspect of the invention, the compounds of the invention may be employed together with at least one other antiviral agent chosen from protease inhibitors, polymerase inhibitors, and helicase inhibitors.

10

In another aspect of the invention, the compounds of the invention may be employed together with at least one other antiviral agent chosen from Interferon- α and Ribavirin.

15 The combinations referred to above may conveniently be presented for use in the form of a pharmaceutical formulation and thus pharmaceutical formulations comprising a combination as defined above together with a pharmaceutically acceptable carrier therefor comprise a further aspect of the invention.

20

The individual components of such combinations may be administered either sequentially or simultaneously in separate or combined pharmaceutical formulations.

25 When the compounds of formula (I) or (Ia) or a pharmaceutically acceptable salts thereof is used in combination with a second therapeutic agent active against the same virus the dose of each compound may be either the same as or differ from that when the compound is used alone. Appropriate doses will be readily appreciated by those skilled in the art.

The following general schemes and examples are provided to illustrate various embodiments of the present invention and shall not be considered as limiting in scope.

35

Example 1

Preparation of 3-(2-Chloro-benzenesulfonylamino)-5-phenyl-thiophene-2-carboxylic acid, compound #29

STEP I

3-Amino-5-phenyl-thiophene-2-carboxylic acid.

To a suspension of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (5 g, 21.459 mmol) in a mixture of THF:MeOH:H₂O (3:2:1, 75 mL), 1N aqueous solution of LiOH.H₂O (64 mL, 64.378 mmol) was added. The reaction mixture was stirred at 85°C (external temperature) for 4h. Solvents were removed under reduced pressure and the residue was partitioned between water and ethyl acetate. The water layer was separated and acidified with 1N HCl solution and then ethyl acetate was added to it. The organic phase was separated, dried (Na₂SO₄) and concentrated to obtain 3-Amino-5-phenyl-thiophene-2-carboxylic acid (4.15 g, 88%) as a yellowish solid. H NMR (DMSO-D₆, 400 MHz): 7.59 (d, 2H), 7.40 (m, 3H), 6.92 (s, 1H).

STEP II

3-(2-Chloro-benzenesulfonylamino)-5-phenyl-thiophene-220 carboxylic acid
3-Amino-5-phenyl-thiophene-2-carboxylic acid (100mg, 0.457 mmol)
was taken in a mixture of dioxane and water (1:1, 25 mL) and
then added sodium carbonate (242 mg, 2.285 mmol) and 1chlorobenzenesulfonyl chloride (289 mg, 1.369 mmol). The
25 reaction mixture was stirred at room temperature for 12 h. Half
of the solvent was removed under reduced pressure and then
diluted with water and ether in a separatory funnel. The ether
layer was separated and the aqueous layer was acidified with 10%
KHSO, solution. Ethyl acetate was added to the aqueous phase to
30 dissolve the white precipitate. The ethyl acetate layer was

WO 02/100851 separated, dried (Na,SO₄) and concentrated to 5 mL. The white solid was filtered and then washed with cold ethyl acetate to obtain 3-(2-Chloro-benzenesulfonylamino)-5-phenyl-thiophene-2-carboxylic acid (125 mg, 69%). 1 H NMR (DMSO-D₆, 400 MHz): 10.51 (bs, 1H), 8.30 (d, 1H), 7.72-7.60 (m, 4H), 7.57 (m, 1H), 7.44 (m, 4H).

The following compounds were prepared in a similar manner as described in general scheme 1:

Compound #3, Compound #5, Compound #7, Compound #13, Compound #15, Compound #16, Compound #17, Compound #18, Compound #21, Compound #22, Compound #23, Compound #29, Compound #30, Compound #34, Compound #37, Compound #38, Compound #39, Compound #40, Compound #41, Compound #42, Compound #44, Compound #45, Compound 15 #46, Compound #49, Compound #50, Compound #52, Compound #53, Compound #54, Compound #55, Compound #76, Compound #94

Example 2

3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid , compound #62

5

STEP I

3-(bis-(Toluene-2-sulfonyl)-amino)-thiophene-2-carboxylic acid methyl ester

- To a cold (0°C) stirred sodium hypochlorite (NaOCl, 10.8% commercial bleach, 124 mL, 180.00 mmol) solution was added othiocresol (2.23 g, 2.12 mL, 18.0 mmol). To this vigorous stirred solution was added conc. Sulfuric acid (caution! extremely exothermic, 92 g, 50 mL, 938 mmol) dropwise. The resultant yellow reaction mixture was stirred for 2 h at the same temperature, diluted with water (50 mL) and dichloromethane 50 mL. The organic solution was separated, aqueous solution was extracted with CH₂Cl₂ (2 x 50 mL). The combined organic extracts were washed with water, brine and dried.
- 20 Evaporation of the solvent under reduced pressure furnished the

2-methylsulfonyl chloride (3.13 g, 91.5% yield), which was used in the next step without purification. ^{1}H NMR (CDCl₃,300 MHz) 8.07 (td, J=7.3, 1.5 Hz, 1H), 7.61 (tt, J=7.5, 1.1 Hz, 1H), 7.44-7.40 (m, 2H), 2.80 (s, 3H).

5

To a stirred solution of the methyl 3-amino-thiophene-2-carboxylic acid (1.0 g, 6.36 mmol) and DMAP (776 mg, 6.36 mmol) in CH₂Cl₂ was sequentially added triethyl amine (1.61 g, 15.9 mmol, 2.5 eq) and o-toluenesulfonyl chloride (3.02 g, 15.9 mmol, 2.5 eq), stirred for 24 h. The reaction mixture was diluted with EtOAc (100 mL), washed with 1.2 N HCl (2 x 50 mL), 6 N HCl (40 mL), saturated NaHCO₃ solution, brine and dried. Evaporation of the solvent under reduced pressure yielded 3-(bis-(Toluene-2-sulfonyl)-amino)-thiophene-2-carboxylic acid methyl ester (2.78 g, 93.3%) as a solid. The crude product was used in the next step without purification. H NMR (CDCl₃,300 MHz) 8.198 (dd, J = 8.0, 1.2 Hz, 2H), 7.52 (d, J = 5.3 Hz, 1H), 7.5 (dt, J = 7.5 Hz, 1.1 Hz, 2H), 7.36 (t, J = 7.5 Hz, 3H), 7.28 (d, J = 7.6 Hz, 2H), 7.16 (d, J = 5.3 Hz, 1H), 3.44 (s, 3H), 2.43 (s, 3H).

20

STEP II

3-(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid

To a stirred mixture of 3-(bis-(Toluene-2-sulfonyl)-amino)
thiophene-2-carboxylic acid methyl ester (2.5 g, 5.35 mmol) in
1,4-dioxane/MeOH/water (3:1:1; 62.5 mL) was added aq. 1 N NaOH

solution (16.05 mL, 16.05 mmol, 3.0 eq) and heated at 85°C for 3.

5 h and it was then cooled to rt. To the reaction mixture was

added 1.2 N HCl (16.0 mL), extracted with CHCl₃ (3 x 30 mL),

washed with brine and dried. Evaporation of the solvent gave 3
(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid (1.5 g,

99%) as a white solid. H NMR (DMSO-d₆,300 MHz) 7.94 (dd, J = 7.9

Hz, 1.3 Hz, 1H), 7.76 (d, J = 5.5 Hz, 1H), 7.55 (dt, J = 7.5 Hz,

1.3 Hz, 1H), 7.42-7.37 (m, 2H), 7.1 (d, J = 5.5 Hz, 1H), 2.57

(s, 3H).

STEP III

3-(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tertbutyl ester

To a cold (-40°C) mixture of 3-(Toluene-2-sulfonylamino)thiophene-2-carboxylic acid (1.5 g, 5.05 mmol) in 1,4dioxane/CHCl, (1:2, 12 mL) was bubbled 2-methyl-2-propene gas (15 5 mL) in a sealed tube. To this was added Conc. H,SO, (0.070 mL, 1.3 mmol) and slowly warmed up to room temperature. The resultant reaction mixture was heated at 70°C for 2.5 days in a sealed tube, cooled to -40°C, stopper was removed. The reaction mixture was slowly brought up to room temperature and stirred 10 until the excess gas is released. The mixture was extracted with EtOAc, washed with aq. NaHCO, solution, brine and dried. Evaporation of the solvent and purification of the residue on silica gel using EtOAc/hexane (1:10) as an eluent furnished 3-(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl 15 ester (1.31 g, 73.5% based on 90% conversion). H NMR (CDCl, ,300 MHz) 9.89 (s, 1H), 8.01 (d, J = 7.9 Hz, 1H), 7.43 (dt, J = 7.5Hz, 1.5 Hz, 1H), 7.3-7.25 (m, 3H), 7.2 (d, J = 5.4 Hz, 1H), 2.69(s, 3H), 1.56 (s, 9H).

20 STEP IV

5-Bromo-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester

To a cold (-30°C) stirred solution of diisopropylamine (1.345 g, 1.86 mL, 13.3 mmol, 3.6 eq) in THF (74.0 mL) was added n-BuLi (1.6 M in hexane, 7.63 mL, 12.21 mmol, 3.3 eq) dropwise and stirred for 20 min. To the cold (-78°C) LDA solution was added a solution of 3-(Toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (1.31 g, 3.7 mmol, 1.0 eq) in THF (20 mL) dropwise and the solution was stirred for 2h at the same temperature. The resultant red colored solution was then quenched with 1,2-dibromotetrafluoroethane (5.77 g, 2.65 mL, 22.2 mmol, 6.0 eq, passed through K,CO, prior to use) in one portion, stirred for 1 h before being added sat. NH,Cl solution (15.0 mL). The reaction mixture was warmed up to rt, extracted with EtOAc, washed with brine and dried. Evaporation of the solvent and purification of the residue over silica gel column furnished 5-Bromo-3-(toluene-2-sulfonylamino)-thiophene-2-

carboxylic acid tert-butyl ester (1.2 g, 75% yield). H NMR (CDCl₃, 300 MHz) 9.72 (s, 1H), 8.0 (dd, J = 7.8, 1.3 Hz, 1H), 7.47 (dt, J = 7.5, 1.2 Hz, 1H), 7.35-7.30 (m, 2H), 7.24 (s, 1H), 2.68 (s, 3H), 1.53 (s, 9H).

5

STEP V

3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid tert-butyl ester

- To the mixture of 4-methylbenzeneboronic acid (38.0 mg, 0.279 mmol) and 5-Bromo-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (40 mg, 0.0925 mmol) in 5:1 mixture of toluene/MeOH (2.0 mL) was added a solution of Pd(PPh₃)₄ (12.0 mg, 0.01 mmol, 10 mol%) in toluene (1.0 mL)

 15 followed by aqueous 2M Na₂CO₃ solution (0.1 mL, 0.2 mmol). The resultant reaction mixture was heated at 70°C for 16 h, cooled to room temperature, filtered off through MgSO₄ and washed with EtOAc. Evaporation of the solvent and purification of the residue over preparative TLC (1 mm, 60A°) using ethyl
- 20 acetate/hexane (1:10) as an eluent furnished 3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid tert-butyl ester (36.0 mg, 81% yield). H NMR (CDCl₃, 300 MHz) 9.94 (s, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.44-7.25 (m, 6H), 7.18 (d, J = 8.1 Hz, 2H), 2.71 (s, 3H), 2.36 (s, 3H), 1.56 (s, 9H).

25

STEP VI

3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid

To a stirred solution of 3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid tert-butyl ester (36.0 mg, 0.081 mmol) in CH₂Cl₂ (1.0 mL) was added TFA (0.5 mL), stirred for 1 h at room temperature and diluted with hexane. Evaporation of the solvent under reduced pressure gave essentially the pure product as a solid. The product was purified by triturating with hexane/CH₂Cl₂ furnished 3-(Toluene-2-sulfonylamino)-5-p-tolyl-thiophene-2-carboxylic acid (28.0 mg, 89% yield). H NMR (DMSO-d₆, 300 MHz) 10.21 (br s, 1H), 8.06 (d, J = 7.9 Hz, 1H), 7.56-7.36 (m, 6H), 7.24 (d, J = 7.9 Hz, 2H), 2.59 (s, 3H), 2.48 (s, 3H).

The following compounds were prepared in a similar manner as described in general scheme 2:

5 Compound #6, Compound #8, Compound #11, Compound #14, Compound #24, Compound #56, Compound #57, Compound #58, Compound #59, Compound #60, Compound #62, Compound #63, Compound #64, Compound #65, Compound #66, Compound #67, Compound #68, Compound #69, Compound #70, Compound #71, Compound #552, Compound #79, Compound #80, Compound #81, Compound #83, Compound #84, Compound #85, Compound #86, Compound #87, Compound #88, Compound #89, Compound #90, Compound #91

Example 3

3-(4-Choro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid compound #72

STEP I

3-(4-Chloro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester

5 To mixture of methyl-3-amino-5-phenylthiophene-2-carboxylate (100 mg, 0.428 mmol) in anhydrous pyridine (4.3 ml) was added p-chlorobenzoyl chloride (71 μl, 0.556 mmol). The mixture was stirred for 3 hours at room temperature and concentrated.

Purification chromatography (silica gel, hexane to hexane: ethyl acetate; 95:5) gave 145 mg (91% yield) of 3-(4-Chlorobenzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester.

¹H NMR (CDCl₃, 400 MHz) 8.54(s, 1H), 7.99-7.96 (m, 2H), 7.73-7.71 (m, 2H), 7.52-7.50 (m, 2H), 7.46-7.39 (m, 3H), 3.95 (s, 3H).

15

STEP II

3-(4-Chlorobenzoylamino)-5-phenyl-thiophene-2-carboxylic acid

To a mixture of 3-(4-Chloro-benzoylamino)-5-phenyl-thiophene-2-20 carboxylic acid methyl ester (30 mg, 0.081 mmol) in 1 ml of a 3:2:1 solution made with tetrahydrofuran, methanol and water respectively was added lithium hydroxide monohydrated (20 mg, 0.484 mmol). The mixture was stirred 30 minutes at 60°C, cooled to room temperature, diluted with water and washed with ether 25 (2x). The collected aqueous layer was then acidified with KHSO, 20% to pH 3 and extracted with ethyl acetate (3x). The combined ethyl acetate layers were washed with brine, dried (Na,SO,) and concentrated. The resulting crude was taken in ethyl acetate and reexctracted with NaOH 0.5 N (2x). The combined aqueous layers 30 were then back-washed with ethyl acetate and acidified to pH3 with KHSO, 20% and back-extracted with ethyl acetate (2x). combined organic layers were washed with brine and dried (Na_2SO_4) . ¹H NMR (DMSO-d₆, 400 MHz) 8.35 (s, 1H), 8.02-7.99 (m, 2H), 7.71-7.68 (m, 2H), 7.56-7.53 (m, 2H), 7.43-7.39 (m, 2H), 35 7.35-7.31 (m, 1H).

The following compounds were prepared in a similar manner as described in example 3:

Compound #74, Compound #77, Compound #92, Compound #96;

Example 4

3-(Benzoyl-methyl-amino)-5-phenyl-thiophene-2-carboxylic acid; compound #550

STEP I

3-Methylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester

- To a mixture of methyl-3-amino-5-phenylthiophene-2-carboxylate (200 mg, 0.855 mmol) in anhydrous N,N-dimethylformamide (4.6 ml) were added 4.2 ml (8.55 mmol) of 2M iodomethane solution in t-buthylmethylether. The mixture was stirred at 60°C for 18 hours, concentrated and purified using biotage technics (silica gel,
- hexane to hexane:ethyl acetate;95:5 containing few drops of triethylamine) to give 68 mg (32% yield) of 3-methylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester. H NMR (CDCl₃, 400 MHz) 7.65-7.62 (m, 2H), 7.42-7.36 (m, 3H), 6.86 (broad s, 1H), 3.83 (s, 3H), 3.04 (d, 3H)

STEP II

3-(Benzoyl-methyl-amino)-5-phenyl-thiophene-2-carboxylic acid methyl ester

This compound was prepared in a similar manner as for Example 3, Step I; 3-(Benzoyl-methyl-amino)-5-phenyl-thiophene-2-carboxylic acid methyl ester was obtained 'H NMR (CDCl₃, 400 MHz) 7.60-7.49 (m, 2H), 7.47-7.35 (m, 5H), 7.28-7.20 (m, 3H), 7.11 (broad s, 1H), 3.83 (s, 3H), 3.44 (s, 3H)

20

STEP III

3-(Benzoyl-methyl-amino)-5-phenyl-thiophene-2-carboxylic acid

This compound was prepared in a similar manner as in Example 3, step II; 3-(Benzoyl-methyl-amino)-5-phenyl-thiophene-2-carboxylic acid was obtained; H NMR (CD₃OD, 400 MHz) 7.64-7.62 (m, 2H), 7.47 (s, 1H), 7.44-7.36 (m, 5H), 7.29-7.20 (m, 3H), 3.42 (s, 3H)

The following compounds were prepared in a similar manner as described in example 4:

Compound #9; Compound #73 Compound #75; Compound #75; Compound #78; Compound #93; Compound #95,

15

Example 5

{[5-Phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid , compound #551

20 STEP I

{[5-Phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid methyl ester

To a mixture of 5-phenyl-3-(toluene-4-sulfonylamino)-thiophene25 2-carboxylic acid (prepared according to example 2) (50 mg,
0.134 mmol) in anhydrous dimethylformamide (1.4 ml) were added
HATU 152 mg, 0.402 mmol), glycine methyl ester hydrochloride
(20 mg, 0.161 mmol) followed by collidine (124µl, 0.938 mmol).
The mixture was stirred at room temperature for 1 hour,
30 concentrated and pre-absorbed on SiO₂. Purification
chromatography (hexane to hexane: ethyl acetate; 6:4 to
dichloromethane: methanol;95:5) gave 47 mg of a mixture of {[5Phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}acetic acid methyl ester and collidine. H NMR (CDCl₃, 400 MHz)

WO 02/100851 PCT/CA02/00876
7.76-7.73 (m, 2H), 7.61 (s, 1H), 7.57-7.54 (m, 2H), 7.42-7.36

(m, 3H), 7.24-7.22 (m, 2H), 6.19-6.17 (m, 1H), 4.14-4.12 (m, 2H), 3.79 (s, 3H), 2.35 (s, 3H).

5 STEP II

{[5-Phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid

Following the procedure described for example 3 (STEP II), 28 mg (88% yield) of {[5-phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid were isolated from 33 mg (0.075 mmol) of the {[5-Phenyl-3-(toluene-4-sulfonylamino)-thiophene-2-carbonyl]-amino}-acetic acid methyl ester. H NMR (CD3OD, 400 MHz): 7.73-7.71 (m, 2H), 7.63-7.61 (m, 2H), 7.54 (s, 1H), 7.45-7.39 (m, 3H), 7.33-7.31 (m, 2H), 4.88 (s, 2H), 2.36 (s, 3H).

Example 6

3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid Compound #48

20 .

STEP I

3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester

25 Sodium hydride (60% dispersion in oil, 180 mg, 4,72 mmol) was added to an ice-cold solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (1000 mg, 4,29 mmol) in 25 ml of dimethylformamide in an atmosphere of N₂. After 5 min, 2,4-dichloro-1-chloromethyl-benzene (755 mg, 3,86 mmol) was added to the solution and then the reaction mixture was stirred for 30 min at 0°C and 30 min at room temperature. The mixture was partitioned between ether (20 mL) and water (20 mL) and the organic layer was separated. The aqueous phase was washed twice

with ether (2X20 mL) and the combined ether layer was dried (MgSO₄) and concentrated. The residue obtained was then purified by precipitation. The crude product was taken in 25 ml of ethyl acetate, a yellow precipitate came out which was filtered to obtain 3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester, 835 mg (55%). H-NMR (DMSO,400 MHz): 7,67 ppm (m, 2H, H_{aro}); 7,44-7,35 ppm (m, 6H, H_{aro}); 7,26 ppm (s, 1H, H_{aro}); 4,63 ppm (d, 2H, N-CH₂); 3,75 ppm (s, 3H, O-CH₃)

- 10 STEP II

 3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid
- 3-(2,4-Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic

 acid methyl ester (70 mg, 0,18 mmol) was dissolved in a mixture
 of THF-MeOH-H₂O (3:2:1) (20 mL) and then 1080 ul of LiOH 1N was
 added to it. After 16 h of stirring at temperature of 100°C,
 solvents were removed and then partitioned between 10 ml of H₂O,
 2 ml of KHSO₄ 5% and 10 ml of EtOAc. The organic layer was
 separated and the aqueous phase was washed twice with ethyl
 acetate (2 X 10 mL). The combined ethyl acetate layer was dried
 (MgSO4) and concentrated to obtain 43 mg (63%) of 3-(2,4Dichloro-benzylamino)-5-phenyl-thiophene-2-carboxylic acid ¹H-NMR
 (DMSO, 400 MHz):δ 7,65 ppm (m, 3H, H_{aro}); 7,43-7,32 ppm (m, 5H,

 15 H_{aro}); 7,23 ppm (s, 1H, H_{aro}); 4,61 ppm (d, 2H, N-CH₂).

Example 7

3-{(2,4-Dichloro-benzoyl)-[5-(3-trifluoromethyl-phenyl)-furan-2ylmethyl]-amino}-5-phenyl-thiophene-2-carboxylic acid, Compound #4

STEP I

5

20

5-Phenyl-3-{[5-(3-trifluoromethyl-phenyl)-furan-2-ylmethyl] amino}-thiophene-2-carboxylic acid methylester

10 To a stirred solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (100 mg, 0.416mmol) in dichloromethane (15 mL) were added 5-(trifluoromethyl-phenyl)-furan-2-carbaldehyde (100 mg, 0.429 mmol) and molecular sieves. The reaction mixture was stirred at room temperature overnight. The solution was filtered over celite and the filtrate was evaporated under reduced pressure. The residue was dissolved in anhydrous methanol (15 mL). and cooled to 0°C in an ice bath. Sodium borohydride (18 mg, 1.1 eq.) was added. The reaction mixture was stirred at this temperature for 2 h. Saturated ammonium chloride (10 mL) was added and stirring was continued for an additional 15 min. at room temperature . Methanol was removed and the resulted mixture was extracted with dichloromethane (3 x 30 mL). The organic solution was washed with water, brine and was dried over sodium sulfate. Solvent was evaporated and the crude product was purified on 25 silica gel using hexane : ethylacetate 9:1 as eluent to provide the desired product in 34% yield (65 mg).

¹HNMR(CDC13, 400MHz): 7.80 (s, 1H), 7.73 (m, 1H), 7.55 (m, 2H), 7.41 (m, 2H), 7.33 (m, 3H), 6.93 (s, 1H), 6.48 (d, 1H), 6.24 (d,

1H), 4.43 (s, 2H), 3.76 (s, 3H).

STEP II

3-{(2,4-Dichloro-benzoyl) -[5-(3-trifluoromethyl-phenyl)-furan-2-5 ylmethyl]-amino}-5-phenyl-thiophene-2-carboxylic acid methyl ester

To a stirred solution of 5-Phenyl-3-{[5-(3-trifluoromethyl-phenyl)-furan-2-ylmethyl]-amino}-thiophene-2-carboxylic acid methylester (65 mg 0.142 mmol) in dichloromethane (3 ml) and saturated NaHCO, solution (3 ml) was added a solution of 2,4-dichloro-benzoyl chloride (36 mg, 1.2 eq.) in dichloromethane (0.9 ml). The reaction mixture was stirred vigorously at room temperature for overnight. The organic phase was collected and the aqueous phase was extracted twice with methylene chloride (2 x 15 ml). The organic layers were combined, washed with water, brine and dried over anhydrous Na₂SO₄. Solvent was removed and residue was purified on silica gel using Hexane: EtOAc 9:1 as eluant to give the desired product in 78% yield (70 mg). The proton NMR indicated the presence of rotamers.

20

¹HNMR(CDCl₃, 400MHz): 7.80 (s, 1H), 7.73 (m, 1H), 7.55 (m, 2H), 7.45 (m, 2H), 7.33 (m, 3H), 7.20 (m, 2H), 7.12 (m, 1H), 6.93 (s, 1H), 6.62 (d, 1H), 6.42 (d, 1H), 5.60 (bd, 1H), 4.70 (bd, 1H), 3.76 (s, 3H).

25

STEP III

3-{(2,4-Dichloro-benzoyl) -[5-(3-trifluoromethyl-phenyl)-furan-2-ylmethyl]-amino}-5-phenyl-thiophene-2-carboxylic acid

30 3-{(2,4-Dichloro-benzoyl) -[5-(3-trifluoromethyl-phenyl)-furan-2-ylmethyl]-amino}-5-phenyl-thiophene-2-carboxylic acid methyl ester (62 mg, 0.098 mmol) was dissolved in THF (5 mL) and water (2 mL). A solution of lithium hydroxide (13 mg, 3eq. in 2 mL of water) was added dropwise. After first few drop, a pink color appeared and disappeared. Mixture was stirred for 5 hrs and acidified with 1N HCl-solution. The product was extracted into ethyl acetate, washed once with water, dried over magnesium sulfate. Solvent was evaporated and the residue was purified on silica gel (Bond-Elute 2 g). The product was elute with a 20 mL gradient of Hexane:EtOAc 9:1. 4:1, 7:3, 3:2, 1:1, 2:3 and EtOAc to give the desired product

WO 02/100851 in 76% yield (46 mg).

PCT/CA02/00876

¹HNMR(CD₃OD, 400MHz): 7.90 (s, 1H), 7.83 (m, 1H), 7.55 (m, 2H), 7.40-7.20_(m, 8H), 7.10 (s, 1H), 6.82 (d, 1H), 6.42 (d, 1H), 5.60 (bd, 1H), 4.70 (bd, 1H), 3.86 (s, 3H).

Example 8

Preparation of 3-[(4-Chloro-2,5-dimethyl-benzenesulfonyl)-(3-iodo-benzyl)-amino]-5-phenyl-thiophene-2-carboxylic acid

Compound #1 and 3-[(3-Benzofuran-2-yl-benzyl)-(4-chloro-2,5-dimethyl-benzenesulfonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid compound #2.

STEP I

15

To a solution of 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester (100 mg, 0.229 mmol) in anhydrous DMF (6 mL), 3-iodobenzyl bromide (82 mg, 0.276 mmol) and cesium carbonate (88 mg, 0.276 mmol) were added and the reaction mixture was stirred at room temperature under a N_2 atmosphere for 12 h. The reaction mixture was partitioned between water and ether. The ether layer was separated, dried (Na_2SO_4),

concentrated. The residue was purified by silica gel column chromatography using ethyl acetate and hexane (1:3) as eluent to obtain 3-[(4-Chloro-2,5-dimethyl-benzenesulfonyl)-(3-iodo-benzyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (130 mg, 87%) as a syrup.

STEP II

3-[(4-Chloro-2,5-dimethyl-benzenesulfonyl)-(3-iodo-benzyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (25 mg, 0.038 10 mmol) was taken in a mixture of THF: MeOH: H₂O (3:2:1, 3 mL) and then added 1N aqueous solution of LiOH.H,0 (0.24 mL, 0.228 mmol). The reaction mixture was stirred at room temperature for 12 h. Solvents were removed and the residue was partitioned between water and ethyl acetate. The aqueous layer was acidified using 10 % KHSO, solution. The organic layer was separated, dried (Na.SO.) 15 and concentrated. The residue was purified by silica gel column chromatography using dichloromethane and methanol (9:1) to obtain 3-[(4-Chloro-2,5-dimethyl-benzene-sulfonyl)-(3-iodo-benzyl)amino]-5-phenyl-thiophene-2-carboxylic acid (22 mg, 88%) as a white solid. H NMR (CDCl, 400 MHz): 7.69 (m, 3H), 7.57 (m, 3H), 7.42 (m, 3H), 7.33 (d, 1H), 7.16 (s, 1H), 6.04 (dd, 1H), 4.90 (bs, 2H), 2.36 (s, 6H).

Compound #5 was prepared in a similar manner;

25

3-[(3-Benzofuran-2-yl-benzyl)-(4-chloro-2,5-dimethyl-benzenesulfonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid compound #2

30 STEP I

To a degassed solution of 3-[(4-Chloro-2,5-dimethyl-benzenesulfonyl)-(3-iodo-benzyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (110 mg, 0.169 mmol) and benzofuran-2-boronic acid (55 mg, 0.185 mmol) in a mixture of DME (8 mL) and 2M aqueous Na₂CO₃ (4 mL), Pd(PPh₃)₄ (9 mg) was added and the reaction mixture was stirred at reflux conditions for 2h under a N₂ atmosphere. The reaction mixture was diluted with ethyl acetate and water. The organic layer was separated, dried (Na₂SO₄) and concentrated. 3-[(3-Benzofuran-2-yl-benzyl)-40 (4-chloro-2,5-dimethyl-benzenesulfonyl)-amino]-5-phenyl-

WO 02/100851 PCT/CA02/00876 thiophene-2-carboxylic acid methyl ester (107 mg, 100%) was isolated as a thick syrup and used for the next reaction without any further purification.

5 STEP II

3-[(3-Benzofuran-2-yl-benzyl)-(4-chloro-2,5-dimethylbenzenesulfonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (20 mg, 0.031 mmol) was taken in a mixture of THF: MeOH: H,O (3:2:1, 3 mL) and then added 1N aqueous solution of 10 LiOH.H.O (0.20 mL, 0.186 mmol). The reaction mixture was stirred at room temperature for 12 h. Solvents were removed and the residue was partitioned between water and ethyl acetate. The aqueous layer was acidified using 10 % KHSO, solution. The organic layer was separated, dried (Na,SO,) and concentrated. The 15 residue was purified by silica gel column chromatography using dichloromethane and methanol (9:1) to obtain 3-[(3-Benzofuran-2yl-benzyl)-(4-chloro-2,5-dimethyl-benzene-sulfonyl)-amino]-5phenyl-thiophene-2-carboxylic acid (14 mg, 70%) as a white solid. ^{1}H NMR (DMSO, 400 MHz): $\delta 7.93$ (s, 1H), 7.84 (s, 1H), 7.74(bd, 1H), 7.65-7.22 (m, 14H), 4.95 (s, 2H), 2.33, 2.23 (2s, 6H). 20

Example 9

3-[(4-Chloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid compound #210 .

STEP I

Method A

A DMF (15 mL) solution of 3-Amino-5-phenyl-thiophene-2
5 carboxylic acid methyl ester (500 mg, 21.5 mmol) was cooled to 0

OC and then isopropyl iodide (2.57 mL) and NaH (60%, 775 mg, 32.3 mmol) were added under an atmosphere of N2. The ice bath was removed and the reaction mixture was stirred at room temperature for 1h. The mixture was partitioned between ether and water, the ether layer was separated, dried (Na2SO4) and concentrated. The residue was purified by silica gel column chromatography using ethyl acetate and hexane (5:95) as eluent to obtain 3-isopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester (189 mg, 32%) as a solid. H NMR (CDCl3, 400 MHz): 7.62 (d, 2H), 7.40 (m, 3H), 6.91 (s, 1H), 3.84 (s, 3H), 1.35 (d, 6H).

Method B

To a stirred solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (1.82 g, 7.8 mmol) in 1,2-dichloroethane (40 mL) was added sequentially 2-methoxypropene (3.0 mL, 31.2 mmol), AcOH (1.8 mL, 31.2 mmol) and NaBH(OAc)₃ (3.31 g, 15.6 mmol) and stirred for 2 hrs. It was then diluted with EtOAc and H₂O. The aqueous solution was adjusted to pH = 7 by adding NaHCO₃. The aqueous phase was extracted with EtOAc, the combined extract was washed with brine and dried on MgSO4 and filtered. Purification on bond elute with hexane to 5% EtOAc-hexane furnished 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (2.07 g, 96% yield).

The intermediate compounds 3-Cyclohexylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester, 3-(1-Methyl-piperidin-4-

ylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester and 3-(1-Methyl-piperidin-4-ylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester were prepared in a similar manner as described and used as intermediates in the synthesis of compound #543, compound #553 and compound #573

20 STEP II

To a suspension of 3-isopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester (1.2 g, 4.364 mmol) in a mixture of $\rm H_{2}O$ (22 mL) and dioxane (35 mL), 1N aqueous solution of NaOH (13 mL, 13.00 mmol) was added. The reaction mixture was stirred at $100^{10}C$ for 3h. The reaction mixture was used for the next reaction without any further purification.

To this reaction mixture of 3-Amino-5-phenyl-thiophene-2-carboxylic acid sodium salt (23 mL, 1.41 mmol), 4-chlorobenzoyl chloride (0.269 mL, 2.11 mmol) was added at 0°C. The pH of the solution was maintained at 9 by adding 1N NaOH solution and then stirred at room temperature for 5h. The reaction mixture was diluted with ethyl acetate and water. The water layer was acidified by adding 1N HCl solution. The organic layer was separated, dried (Na₂SO₄) and concentrated. The crude product was

purified by recrystallization from ethyl acetate to obtain the pure 3-[(4-Chloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid (45 mg) as a white solid. ¹H NMR (DMSO-D₆, 400 MHz): 7.58 (d, 2H), 7.38-7.26 (m, 6H), 7.13 (d, 1H), 4.77 (m, 1H), 1.25 (d, 3H), 1.02 (d, 3H). ESI (M-H): 398.

Similarly, the following compounds were made: Compound #218 ,
Compound #219 , Compound #226 , Compound #234 , Compound #243 ,
Compound #246 , Compound #250 , Compound #262 , Compound #324 ,
Compound 326 , Compound #331 .

Example 10

15

3-[(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid compound #149

NH₂ CI

Step I

20

3-(2,4-Dichloro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester.

To a ice-cold solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester 1 (5 g, 21.5 mmol) and triethylamine (4.56 g, 45.0 mmol) in dichloromethane (100 ml)

was added 2,4-dichlorobenzoyl chloride (3.90 g, 19.4 mmol). The reaction mixture was stirred for 30 min a 0°C and 16 h at room temperature. Then, the reaction mixture was partitioned between 25 ml of H₂O, 50 ml sat. NaHCO₃ and 50 ml of CH₂Cl₂. The organic layer was separated and the aqueous phase was washed twice with CH₂Cl₂ (2 X 50 mL). The combined dichloromethane layer was dried (MgSO₄), concentrated and the residue was purified by recrystallization in CH₂Cl₂ to obtain 5.832 g (74%) as a white solid of 3-(2,4-Dichloro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester. NMR ¹H (CDCl₃, 400 MHz): 8,30 ppm (s, 1H, H_{aro}); 7,74-7,66 ppm (m, 3H, H_{aro}); 7,51 ppm (d, 1H, H_{aro}); 7,46-7,34 ppm (m, 4H, H_{aro}); 3,91 ppm (s, 3H).

Step II

3-[(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester.

Sodium Hydride (60% dispersion in oil, 190 mg, 5,2 mmol) was added to an ice-cold solution of 3-(2,4-Dichloro-benzoylamino)-5-phenyl-thiophene-2-carboxylic acid methyl ester (2) (1.5 g, 3,69 mmol) in 350 ml of N,N-dimethylformamide in an atmosphere of N_2 . After 5 min, 2-Iodo-propane (941 mg, 5.54 mmol) was added to the solution and then the reaction mixture was stirred for 30 min at 0°C and 64 h at room temperature. The mixture was partitioned between ether (200 mL) and water (350 mL) and the organic layer was separated. The aqueous phase was washed twice with ether (2 X 70 mL) and the combined ether layer was dried (MgSO₄), concentrated and the residue was purified by flash chromatography (10% EtOAc/Hexane) to obtain 908 mg (55%) of 3-30 [(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2carboxylic acid methyl ester. NMR ¹H (CDCl₃, 400 MHz): Rotamere 95/05 : 7,54 ppm (dd, 2H, H_{aro}); 7,49-7.35 ppm (m, 3H, H_{aro}); 7,29-7,25 ppm (m, 2H, H_{aro}); 7,15 ppm (d, 1H, H_{aro}); 7,05 ppm (d, ... 1H, H_{aro}) 5,09 ppm (hex, 1H, $N-CH(CH_3)$, major rotamere); 3,99 ppm 35 (hex, $N-CH(CH_3)$, minor rotamere); 3,89 ppm (s, 3H); 1,40 ppm (d,

3H, N-CH(CH₃), major rotamere); 1,28 ppm (d, N-CH(CH₃), minor rotamere); 1,09 ppm (d, 3H, N-CH(CH₃), major rotamere); 1,01 ppm (d, N-CH(CH₃), minor rotamere).

5 Step III ·

3-[(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid.

3-[(2,4-Dichloro-benzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-10 carboxylic acid methyl ester (3) (345 mg, 0.77 mmol) was dissolved in a mixture of THF-MeOH- H_2O (3:2:1) (30 mL) and then 4,6 ml of LiOH 1N was added to it. After 120 min of stirring at room temperature, solvant was removed and then partitioned between 25 ml of $\rm H_2O$, 4 ml of $\rm KHSO_4$ 5% and 25 ml of $\rm EtOAc$. The 15 organic layer was separated and the aqueous phase was washed twice with ethyl acetate (2 X 10 mL). The combined ethyl acetate layer was dried (MgSO₄), concentrated and the residue was purified by preparative chromatography (10% MeOH/CH2Cl2) to obtain 175 mg (53%) as a white solid of 3-[(2,4-Dichlorobenzoyl)-isopropyl-amino]-5-phenyl-thiophene-2-carboxylic acid. NMR 1 H (DMSO, 400 MHz): Rotamer 95/05 : 7,82 ppm (m, H_{aro} , minor rotamer); 7,69 ppm (d, 2H, H_{aro}); 7,61 ppm (d, 1H, H_{aro}); 7,51-7,37 ppm (m, 4H, H_{aro}); 7,35-7,28 ppm (m, 2H, H_{aro}); 4,89 ppm (hex, 1H, N-CH(CH₃), major rotamer); 3,84 ppm (hex, N-CH(CH₃), 25 minor rotamer); 1,36 ppm (d, 3H, N-CH(CH_3), major rotamer); 1,25 ppm (d, N-CH(CH_3), minor rotamer); 1,03 ppm (d, 3H, N-CH(CH_3), major rotamer); 0,93 ppm (d, N-CH(CH_3), minor rotamere).

The following compounds were prepared in a similar manner:

30 Compound #201 , Compound #204 , Compound #233 , Compound #244 ,

Compound #261 , Compound #264 , Compound #299 .

Example 11

3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2-35 carboxylic acid. Compound #208.

Step I

5-Phenyl-3-phenylamino-thiophene-2-carboxylic acid methyl ester.

5

To a solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (1 g, 4.29 mmol) in dichloromethane (50 ml) was added phenyl boronic acid (1.05 g, 8.6 mmol), pyridine (680 mg, 8.6 mmol) and copper(II) acetate (1.18 g, 6.5 mmol). The reaction mixture was stirred for 16 h at room temperature. Then, the reaction mixture was filtered through celite, concentrated and the residue was purified by flash chromatography (9:1 Hexane/EtOAc) to obtain 435 mg (33%) of 5-Phenyl-3-phenylamino-thiophene-2-carboxylic acid methyl ester. NMR ¹H (CDCl₃, 400 MHz): 7,38 ppm (dd, 2H, H_{aro}); 7,35-7,26 ppm (m, 5H, H_{aro}); 7,19 ppm (s, 1H, H_{aro}); 7,15 ppm (dd, 2H, H_{aro}); 7,02 ppm (ddt, 1H, H_{aro}); 3,82 ppm (s, 3H).

Step II

3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester.

Sodium Hydride (60% dispersion in oil, 80 mg, 1,5 mmol) was added to an ice-cold solution 5-Phenyl-3-phenylamino-thiophene-2-carboxylic acid methyl ester (2) (230 mg, 0,74 mmol) in 20 ml of N,N-dimethylformamide in an atmosphere of N2. After 5 min, 2,4-Dichloro-benzoyl chloride (310 mg, 1.48 mmol) was added to the solution and then the reaction mixture was stirred for 30 min at 0°C and 16 h at room temperature. The mixture was partitioned between ether (20 mL) and water (20 mL) and the organic layer was separated. The aqueous phase was washed twice with ether (2 X 10 mL) and the combined ether layer was dried (MgSO4), concentrated and the residue was purified by preparative chromatography (30% EtOAc/Hexane) to obtain 58 mg (16%) of 3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester. NMR ¹H (CDCl3, 400 MHz): 7,65-7,10 ppm (m, 14H, Haro); 3,77 ppm (s, 3H).

Step III

3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2-carboxylic acid.

20

3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenyl-thiophene-2carboxylic acid methyl ester (55 mg, 0.11 mmol) was dissolved in
a mixture of THF-MeOH-H₂O (3:2:1) (15 mL) and then 0.66 ml of
LiOH 1N was added to it. After 60 min of stirring at room

25 temperature, solvents were removed and then partitioned between
15 ml of H₂O, 4 ml of KHSO₄ 5% and 15 ml of EtOAc. The organic
layer was separated and the aqueous phase was washed twice with
ethyl acetate (2 X 10 mL). The combined ethyl acetate layer was
dried (MgSO₄), concentrated and the residue was purified by

30 preparative chromatography (10% MeOH/CH₂Cl₂) to obtain 32 mg
(60%) of 3-[(2,4-Dichloro-benzoyl)-phenyl-amino]-5-phenylthiophene-2-carboxylic acid. NMR ¹H (DMSO, 400 MHz): Rotamer:
7,75 ppm (d, 1H, H_{aro}); 7,68 ppm (2H, H_{aro}); 7,53 ppm (d, H_{aro},
minor rotamer); 7,51-7.23 ppm (m, 11H, H_{aro}, minor rotamer); 7,17

Compound #525 was prepared in a similar manner.

Example 12

5 3-[tert-Butyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid compound #327

Step I

3-tert-Butylamino-5-phenyl-thiophene-2-carboxylic acid methyl
ester.

Concentrated sulfuric acid (10 drop) was added to a solution of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (500 mg, 2,15 mmol) in 20 ml of dioxane/chloroforme (2:3) in a sealed tube. After cooling the solution at -78 °C, put 20 ml of isobutene gaz. The sealed tube was closed and then the reaction mixture was stirred for 6 days at 60 °C. The solvant was removed and then partitioned between 15 ml of sat. Na₂CO₃ solution and 15 ml of EtOAc. The organic layer was separated, the aqueous phase was washed twice with ethyl acetate and the combined ethyl acetate layer was dried (MgSO₄), concentrated and the residue was purified by flash chromatography (5% EtOAc/Hexane) to obtain 385 mg (62%) of 3-tert-Butylamino-5-phenyl-thiophene-2-carboxylic

5 Step II

3-[tert-Butyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester.

To a solution of 3-tert-Butylamino-5-phenyl-thiophene-2
10 carboxylic acid methyl ester (100 mg, 0.35 mmol) in'

dichloroethane (10 ml) in an atmosphere of N₂ was added 2,4
dichloro-benzoyl chloride (79 mg, 0.38 mmol). The reaction

mixture was stirred for 16 h at reflux. Then, the solvents were

removed and the residue was purified by flash chromatography

15 (9:1 Hexane/EtOAc) to obtain 112 mg (69%) of 3-[tert-Butyl
(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic

acid methyl ester. NMR ¹H (CDCl₃, 400 MHz): 7,50 ppm (m, 2H,

H_{aro}); 7,44-7,34 ppm (m, 3H, H_{aro}); 7,27 ppm (s, 1H, H_{aro}); 7,18

ppm (dl, 1H, H_{aro}); 7,14 ppm (d, 1H, H_{aro}); 7,00 ppm (dd, 1H,

20 H_{aro}); 3,93 ppm (s, 3H); 1,56 ppm (s, 9H).

Step III

3-[tert-Butyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid.

25

3-[tert-Butyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene2-carboxylic acid methyl ester (112 mg, 0.24 mmol) was dissolved in a mixture of THF-MeOH-H₂O (3:2:1) (15 mL) and then 1.5 ml of LiOH 1N was added to it. After 3 h of stirring at room

30 temperature, solvant was removed and then partitioned between 15 ml of H₂O, 4 ml of KHSO₄ 5% and 15 ml of EtOAc. The organic layer was separated and the aqueous phase was washed twice with ethyl acetate (2 X 10 mL). The combined ethyl acetate layer was dried (MgSO₄), concentrated and the residue was purified by preparative

35 chromatography (10% MeOH/CH₂Cl₂) to obtain 32 mg (29 %) of 3-

[tert-Butyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid. NMR 1 H (DMSO, 400 MHz): 7,62 ppm (d, 2H, $_{\rm Haro}$); 7,44-7,34 ppm (m, 4H, $_{\rm Haro}$); 7,32-7,12 ppm (m, 3H, $_{\rm Haro}$); 2,48 ppm (s, 9H).

5

Example 13

3-[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid. Compound #333

10 Step I

3-Cyclopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester.

To a solution of 3-Bromo-5-phenyl-thiophene-2-carboxylic acid

methyl ester (250 mg, 0.89 mmol) in toluene (25 ml) was added cyclopropylamine (57 mg, 1.0 mmol), cesium carbonate (382 mg, 1.2 mmol), BINAP (50 mg, 0.08 mmol) and tris (dibenzyli-denacetone)dipaladium (0) (38 mg, 0.04 mmol). The reaction mixture was stirred for 16 h at 110 °C in a sealed tube. The

mixture was partitioned between toluene (20 mL) and water (20 mL) and the organic layer was separated. The aqueous phase was

washed twice with toluene (2 X 10 mL) and the combined toluene layer was dried (MgSO₄), concentrated and the residue was purified by preparative chromatography (10% EtOAc/Hexane) to obtain 52 mg (22 %) of 3-Cyclopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester. NMR ¹H (CDCl₃, 400 MHz): 7,67-7,62 ppm (m, 2H, H_{aro}); 7,43-7,32 ppm (m, 3H, H_{aro}); 7,16 ppm (s, 1H, H_{aro}); 3,82 ppm (s, 3H); 2,65 ppm (m, 1H); 0,62 ppm (m, 2H); 0,35 ppm (m, 2H).

10 Step II

3-[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester.

To a solution of 3-Cyclopropylamino-5-phenyl-thiophene-2
carboxylic acid methyl ester (52 mg, 0.19 mmol) in

dichloroethane (10 ml) in an atmosphere of N₂ was added 2,4
dichlorobenzoyl chloride (45 mg, 0.21 mmol). The reaction

mixture was stirred for 16 h at reflux. Then, the solvant was

removed and the residue was purified by flash chromatography

20 (8:2 Hexane/EtOAc) to obtain 85 mg (99%) of 3-[Cyclopropyl
(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2-carboxylic

acid methyl ester. NMR ¹H (CDCl₃, 400 MHz): 7,64 ppm (d, 2H,

H_{aro}); 7,47 ppm (m, 2H, H_{aro}); 7,44-7,33 ppm (m, 3H, H_{aro}); 7,21
7,12 ppm (m, 2H, H_{aro}); 3,89 ppm (s, 3H); 3,33 ppm (m, minor

25 rotamer); 3,13 ppm (m, 1H, major rotamer) 1,01-0,49 ppm (m, 4H).

Step III

3-[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene
2-carboxylic acid.

30 3-[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene2-carboxylic acid methyl ester (85mg, 0.19mmol) was dissolved in a mixture of THF-MeOH-H₂O (3:2:1) (10 mL) and then 1.2 ml of LiOH
1N was added to it. After 60 min of stirring at room temperature, solvant was removed and then partitioned between 15
35 ml of H₂O, 4 ml of KHSO₄ 5% and 15 ml of EtOAc. The organic layer

was separated and the aqueous phase was washed twice with ethyl acetate (2 X 10 mL). The combined ethyl acetate layer was dried (MgSO₄), concentrated and the residue was purified by preparative chromato \overline{graphy} (10% MeOH/CH₂Cl₂) to obtain 22 mg (27%) of 3-

[Cyclopropyl-(2,4-dichloro-benzoyl)-amino]-5-phenyl-thiophene-2carboxylic acid. NMR ¹H (DMSO, 400 MHz): rotamer : 7,75 ppm (m,
2H, H_{aro}); 7,68 ppm (m, H_{aro}, minor rotamer) ; 7,62-7,55 ppm (m,
2H, H_{aro}); 7,52 ppm (m, H_{aro}, minor rotamer) ; 7,48-7.27 ppm (m,
5H, H_{aro}); 3,14 ppm (m, minor rotamer); 3,04 ppm (m, 1H, major
rotamer); 0,87-0,42 ppm (m, 4H,).

The following compounds were prepared in a similar manner: Compound #403 , Compound #404

Example 14

3-[(2,4-dichloro-benzoyl)-piperidin-4-ylmethylamino]-5-phenylthiophene-2-carboxylic acid Compound #519 .

STEP I

20 A suspension of 3-amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (0.70 g, 3 mmol) and 4-formyl N-Cbz-piperidine (0.74 g, 3 mmol) in THF (1.2 mL) was treated with dibutyltin dichloride (46 mg, 0.15 mol) followed by phenylsilane (0.41 mL, 3.3 mmol). The mixture was stirred for 2 days at room

25 temperature. The solvent was then evaporated and the residue was purified by silica gel column chromatography using

CH₂Cl₂:hexanes:EtOAc as eluent to provide 4-[(2-Methoxycarbonyl-5-phenyl-thiophen-3-ylamino)-methyl]-piperidine-1-carboxylic acid benzyl ester (0.6906 g, 50% yield).

5 STEP II

- 4-[(2-Methoxycarbonyl-5-phenyl-thiophen-3-ylamino)-methyl]piperidine-1-carboxylic acid benzyl ester (133 mg ,0.28 mmol) was
 dissolved in 1,2-dichloroethane (2.8 mL) and was treated with 2,4dichlorobenzoyl chloride (60 μL, 0.43 mmol). The solution was
 10 heated at reflux for 1 day. The solvent was then evaporated and
 the residue purified by silica gel column chromatography using
 hexanes:EtOAc as eluent to provide 4-{[(2,4-Dichloro-benzoyl)-(2-
- methoxycarbonyl-5-phenyl-thiophen-3-yl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (0.156 g, 85% yield).

15 STEP III

- 4-{[(2,4-Dichloro-benzoyl)-(2-methoxycarbonyl-5-phenyl-thiophen-3-yl)-amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (150 mg, 0.24 mmol) was dissolved in a mixture of THF:MeOH:H₂O (3:2:1, 2.4 mL) and treated with LiOH.H₂O (29.6 mg, 0.7 mmol). The
- solution was heated at 55 °C for 2 h. The solvents were removed and the residue was acidified using HCl. The product was extracted with EtOAc and the organic layers were washed with brine and dried. The residue was purified by silica gel column chromatography using EtOAc:MeOH:AcOH as eluent to provide 4-{[(2-
- 25 Carboxy-5-phenyl-thiophen-3-yl)-(2,4-dichloro-benzoyl)-amino]methyl}-piperidine-1-carboxylic acid benzyl ester (124 mg, 85%
 yield).

STEP IV

- 4-{[(2-Carboxy-5-phenyl-thiophen-3-yl)-(2,4-dichloro-benzoyl)amino]-methyl}-piperidine-1-carboxylic acid benzyl ester (124
 mg, 0.2 mmol) was dissolved in MeOH (2 mL) and treated with 10%
 Pd/C (200 mg) under H₂ balloon. The reaction was stirred at room
 temperature for 18 h and the mixture was filtered on celite.
- 35 The solution was evaporated to a residue that was purified by

reverse-phase HPLC to provide 3-[(2,4-Dichloro-benzoyl)piperidin-4-ylmethyl-amino]-5-phenyl-thiophene-2-carboxylic acid
(17.3 mg, 18% yield). ¹H NMR (CD₃OD, 300 MHz): 7.55 (d, 1 H),
7.50 (m,-2-H), 7.27-7.39 (m, 4 H), 7.25 (s, 1 H), 7.18 (dd, 1
H), 4.12 (m, 1 H), 3.75 (m, 1 H), 3.43 (m, 2 H), 2.96 (q, 2 H),
2.65 (d, 2 H), 2.05 (m, 1 H), 1.62 (m, 2 H).

The following compounds were prepared in a similar manner:

Compound #503 , Compound #509 , Compound #519 , Compound #529 ,

Compound #537 , Compound #538 , Compound #516 , Compound #522 ,

Compound #535 .

Example 15

3-[Isopropyl-(3-methyl-cyclopent-3-enecarbonyl)-amino]-5 phenyl-15 thiophene-2-carboxylic acid Compound #405

Step I:

To a cold (-78 °C) stirred solution of LDA (generated from DIPA (1.42 mL, 10.14 mmol), BuLi (5.85 mL, 9.36 mmol) in THF at -78°C for 20 min) in THF (31 mL) was added a solution of Pent-4-enoic acid ethyl ester (1.0 g, 7.8 mmol, 1.2 eq.) in THF (9.0 mL). After stirred for 1 h, neat 3-Bromo-2-methyl-propene (2.03 g, 15.0 mmol, 1.51 mL) was added and slowly warmed up to room temperature for overnight. The reaction mixture was then quenched with saturated NH₄Cl solution, extracted with ether, washed with brine and dried. Evaporation of the solution furnished the 2-Allyl-4-methyl-pent-4-enoic acid ethyl ester

(1.45 g, 100%) as an oil which was used in the next step without purification. ^{1}H NMR (400 MHz, CDCl₃), 5.78-5.71 (m, 1H), 5.05 (d, J=18.6 Hz, 1H), 5.02 (d, J=9.4 Hz, 1H), 4.76 (brs, 1H), 4.70 (s, 1H), 4.11 (dq, J=7.2, 1.0 Hz, 2H), 2.66-2.13 (m, 5H), 5 1.72 (s, 3H), 1.23 (dt, J=7.2, 1.3 Hz, 3H).

Step II:

To a refluxing stirred solution of the 2-Allyl-4-methyl-pent-4-enoic acid ethyl ester (364 mg, 2.0 mmol) in CH₂Cl₂ (100 mL, 0.02 M solution) was added drop wise a solution of the tricyclohexylphosphine (1,3-Bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene) (benzylidine) ruthenium (IV) dichloride (85 mg, 0.1 mmol) in CH₂Cl₂ (3.0 mL). After 50 min, the reaction mixture was cooled to room temperature, concentrated and purified on silica gel bond elute using EtOAc/hexane (1:20) as an eluent furnished the 3-Methyl-cyclopent-3-enecarboxylic acid ethyl ester (286 mg, 93% yield) as an oil. H NMR (CDCl₃, 400 MHz), 5.25 (brs, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.2-3.1 (m, 1H), 2.65-2.46 (m, 4H), 1.74 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H).

Step III:

20

A solution of the 3-Methyl-cyclopent-3-enecarboxylic acid ethyl ester (255 mg, 1.65 mmol) in MeOH (4.0 mL) and 10% aq. NaOH (3.3 mL, 8.25 mmol) was heated at 50°C for 16 h, reaction mixture was cooled to room temperature, solvent was evaporated, diluted with water. The aqueous solution was washed with ether, and acidified with aq. 1 N HCl, extracted with ether. The ethereal solution was washed with brine and dried. Evaporation of the solvent furnished the 3-Methyl-cyclopent-3-enecarboxylic acid (200 mg, 97% yield). 1H NMR (CDCl₃, 400 MHz) 5.27 (brs, 1H), 3.26-3.17 (m, 1H), 2.7-2.55 (m, 4H), 1.74 (s, 3H).

Step IV:

The coupling of the 3-Isopropylamino-5-phenyl-thiophene-2-35 carboxylic acid methyl ester (82 mg, 0.3 mmol) and the 3-MethylWO 02/100851

cyclopent-3-enecarboxylic acid (45 mg, 0.357 mmol) using PPh₃

(95.4 mg, 0.363 mmol) and NCS (48.5 mg, 0.363 mmol) furnished the 3-[Isopropyl-(3-methyl-cyclopent-3-enecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (70 mg, 61% yield) ¹H NMR (CDCl₃, 400 MHz 1:1 mixture of rotamers), 7.68-7.64 (m, 4H), 7.5-7.4 (m, 6H), 7.1 (s, 1H), 7.09 (s, 1H), 5.2 (s, 1H), 5.1 (s, 1H), 5.06-4.98 (m, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.08-3.0 (m, 2H), 2.85-2.76 (m, 2H), 2.5-2.42 (m, 2H), 2.3-2.1 (m, 4H), 1.69 (s, 3H), 1.64 (s, 3H), 1.24 (d, J = 6.7 Hz, 3H), 1.23 (d, J = 6.7 Hz, 3H), 1.01 (d, J = 6.9 Hz, 3H), 1.007 (d, J = 6.8 Hz, 3H).

Saponification of 3-[Isopropyl-(3-methyl-cyclopent-3-enecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (50 mg, 0.13 mmol) using LiOH.H₂O (22 mg) as previously described furnished the 3-[Isopropyl-(3-methyl-cyclopent-3-enecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid (30 mg, 62.5% yield) as a solid.

1H NMR (CD3OD, 400 MHz 1:1 mixture of rotamers) 7.73-7.70 (m,
20 4H), 7.47-7.35 (m, 6H), 7.29 (s, 1H), 7.27 (s, 1H), 5.16 (s,
1H), 5.08 (s, 1H), 4.9-4.8 (m, 2H), 3.15-3.05 (m, 2H), 2.76-2.65
(m, 2H), 2.42-2.12 (m, 6H), 1.65 (s, 3H), 1.61 (s, 3H), 1.25 (d,
J = 6.6 Hz, 3H), 1.24 (d, J = 6.6 Hz, 3H), 1.03 (d, J = 6.9 Hz,
6H).

25

Example 16

5-tert-Buty1-3-(2,4-dimethyl-benzenesulfonylamino)-thiophene-2-carboxylic acid Compound #315:

30

STEP I

A mixture of 3-Amino-5-tert-butyl-thiophene-2-carboxylic acid methyl ester (106.5 mg, 0.5 mmol) and 2,4-dimethylsulfonyl chloride (156 mg, 0.75 mmol) in pyridine (1.5 mL) was heated at 72 °C for 16 h. The reaction mixture was diluted with EtOAc, washed with aq. 1N HCl, brine and dried. Evaporation of the solvent and purification of the residue on silica gel bond elute using EtOAc (1:20 to 1:10) as an eluent furnished the 5-tert-Butyl-3-(2,4-dimethyl-benzenesulfonylamino)-thiophene-2-carboxylic acid methyl ester (188 mg, 99% yield). ¹H NMR (CDCl₃,

10 400 MHz) 9.73 (s, 1H), 7.89 (d, J = 8.6 Hz, 1H), 7.04-7.08 (m, 2H), 7.03 (s, 1H), 3.82 (s, 3H), 2.62 (s, 3H), 2.33 (s, 3H), 1.28 (s, 9H).

STEP II

Hydrolysis of the 5-tert-Butyl-3-(2,4-dimethyl-benzenesulfonylamino)-thiophene-2-carboxylic acid methyl ester (55 mg, 0.14 mmol) using LiOH.H₂O (22 mg) as previously described provided the 5-tert-Butyl-3-(2,4-dimethyl-benzenesulfonylamino)-thiophene-2-carboxylic acid (36 mg, 70% yield) as a solid. ¹H NMR (CD₃OD, 400 MHz) 7.85 (d, J = 8.6 Hz, 1H), 7.14-7.10 (m, 2H), 7.0 (s, 1H), 2.56 (s, 3H), 2.31 (s, 3H), 1.27 (s, 9H).

Example 17

5-Benzo[b]thiophen-2-yl-3-(toluene-2-sulfonylamino)-thiophene-2carboxylic acid Compound #230

STEP I

Suzuki coupling of 5-Bromo-3-(toluene-2-sulfonylamino)thiophene-2-carboxylic acid tert-butyl ester (43 mg, 0.1 mmol)

and bezothiophene-2-boronic acid (53.4 mg, 0.3 mmol) was carried out using Pd(PPh₃)₄ and Na₂CO₃ (as described in example 2)
resulted in 5-Benzo[b]thiophen-2-yl-3-(toluene-2-sulfonylamino)thiophene-2-carboxylic acid tert-butyl ester (27 mg, 55% yield).

1 NMR (CDCl₃, 400 MHz) 9.92 (s, 1H), 8.07 (d, J = 7.8 Hz, 1H),

7.79-7.71 (m, 2H), 7.45-7.24 (m, 7H), 2.7 (s, 3H), 1.56 (s, 9H).

STEP II

5-Benzo[b]thiophen-2-yl-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester was hydrolyzed to the acid

15 using TFA as described for example 2 providing 5-Benzo[b]thiophen-2-yl-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid (24 mg, 99% yield). H NMR (DMSO-D6, 400 MHz)

10.19 (s, 1H), 8.0 (d, J = 7.7 Hz, 1H), 7.79-7.74 (m, 1H), 7.86 (s, 1H), 7.84-7.81 (m, 1H), 7.54 (t, J = 7.7 Hz, 1H), 7.53-7.36

20 (m, 4H), 7.32 (s, 1H), 2.58 (s, 3H).

Example 18

5-(1H-Pyrazol-3-yl)-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid Compound #170

25

Step I

To a stirred solution of 5-Bromo-3-(toluene-2-sulfonylamino)thiophene-2-carboxylic acid tert-butyl ester (43mg, 0.1mmol) in toluene (3.0 mL) was sequentially added a solution of Pd(PPh3)4 5 (12 mg, 0.01 mmol) in toluene (1.0 mL) and 3-Trimethylstannanylpyrazole-1-sulfonic acid dimethylamide (prepared according to J. Med. Chem (1998), 41, p-2019) (75 mg, 0.2 mmol, 2.0 eq), and heated the resulting overnight at 80°C. It was then cooled to room temperature, the solvent was evaporated and the crude was 10 purified on preparative TLC using EtOAc/hexane (1:5). 5-(1-Dimethylsulfamoyl-1H-pyrazol-3-yl)-3-(toluene-2-sulfonylamino)thiophene-2-carboxylic acid tert-butyl ester (35 mg, 66.5% yield) was isolated. ¹H NMR (CDCl₃, 400 MHz) 9.93 (s, 1H), 8.11 (d, J = 0.7 Hz, 1H), 8.02 (dd, J = 6.7, 1.32 Hz, 1H), 7.84 (d, J)15 = 0.7 Hz, 1H), 7.45 (dt, J = 7.5, 1.3 Hz, 1H), 7.31 (t, J = 8.2 Hz, 2H), 7.26 (d, J = 1.0 Hz, 1H), 2.98 (s, 6H), 2.7 (s, 3H), 1.55 (s, 9H).

Step II

20 A reaction mixture of 5-(1-Dimethylsulfamoyl-1H-pyrazol-3-yl)-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid tert-butyl ester (10 mg, 0.019 mmol) and 4N HCl (0.3 mL) solution in dioxane in MeOH (0.3 mL) was stirred at room temperature 26 h. Reaction mixture was then diluted with water and extracted with 25 EtOAc, concentrated and purified on preparative TLC using MeOH/CH₂Cl₂/AcOH (5:95:1) furnished the 5-(1H-Pyrazol-3-yl)-3-(toluene-2-sulfonylamino)-thiophene-2-carboxylic acid (4.5 mg, 65.2% yield). ¹H NMR (CD₃OD, 400 MHz) 7.99 (d, J = 7.9 Hz, 1H), 7.81 (s, 1H), 7.43 (t, J = 7.5, 1.3 Hz, 1H), 7.42-7.26 (m, 2H), 7.19 (s, 1H), 2.69 (s, 3H).

Example 19

3-Isopropyl-[(4-methyl-cyclohexanecarbonyl)-amino]-5-m-tolyl-thiophene-2-carboxylic acid Compound #448

STEP I

Trans-4-methyl-cyclohexanecarbonyl chloride was prepared by 5 heating to reflux trans-4-methyl-cyclohexanecarboxylic acid (5g, 0.035 mmol) in thionylchloride (5.0 ml) for 2h followed by purification of the corresponding acyl chloride under reduced pressure in a Kugel-Rhorr apparatus collecting the fraction distilling at 95 °C yielding 5.1 g of the desired material which 10 was used in the next step without further purification. This acyl chloride (1.5 ml, aprox. 10 mmol) was dissolved along with 5-Bromo-3-isopropylamino-thiophene-2-carboxylic acid methyl ester (2 g, 7.12 mmol) in anhydrous dichloroethane (2 mL) and heated at 80 °C (closed vial) for 12h. The solvents were evaporated, the resulting crude material was dissolved in methanol and left 30 min. at room temperature, concentrated and purified via flash chromatography on silica gel using a 5% EtOAc 95% hexanes mixture of eluents, in this manner 600 mg (21%) of 5-Bromo-3-[isopropyl-(4-methyl-cyclohexanecarbonyl)-20 amino]-thiophene-2-carboxylic acid methyl ester the was isolated. 1 H NMR(CDCl₃, 300 MHz): 6.78 (s, 1H), 4.93 (m, 1H), 3.69 (s, 3H), 2.00-1.20 (m, 8H), 1.14 (d, 3H), 0.93 (d, 3H), 0.81 (d, 3H), 0.72-0.70 (m, 2H).

25

STEP II

To a degassed solution of 5-Bromo-3-[isopropyl-(4-methyl-cyclohexanecarbonyl)-amino]-thiophene-2-carboxylic acid methyl ester (100 mg, 0.249 mmol) and 3-methyl boronic acid (38 mg, 0.279 mmol) in a mixture of DME (6 mL) and 2M aqueous Na₂CO₃ (3 mL), Pd(PPh₃)₄ (12 mg) was added and the reaction mixture was stirred at reflux conditions for 12h under a N₂ atmosphere. The reaction mixture was diluted with ethyl acetate and water. The organic layer was separated, dried (Na₂SO₄), concentrated. The residue was purified by column chromatography using ethyl acetate and hexane (1:3) as eluent. 35 mg (34%) of 3-Isopropyl-[(4-methyl-cyclohexanecarbonyl)-amino]-5-m-tolyl-thiophene-2-carboxylic acid methyl ester was isolated. ¹H NMR (CDCl₃, 400 MHz): 7.45 (bs, 2H), 7.36 (t, 1H), 7.23 (m, 1H), 7.01 (s, 1H), 4.99 (m, 1H), 3.83 (s, 3H), 2.41 (s, 3H), 2.01-0.61 (m, 20H).

15 ·

Step III

3-Isopropyl-[(4-methyl-cyclohexanecarbonyl)-amino]-5-m-tolylthiophene-2-carboxylic acid methyl ester (30 mg, 0.073 mmol) was taken in a mixture of THF: MeOH: H2O (3:2:1, 3 mL) and then added 20 1N aqueous solution of LiOH. H_2O (0.44 mL, 0.438 mmol). The reaction mixture was stirred at room temperature for 12 h. Solvents were removed and the residue was partitioned between water and ethyl acetate. The aqueous layer was acidified using 10 % KHSO4 solution. The organic layer was separated, dried 25 (Na₂SO₄) and concentrated. The residue was purified by preparative TLC using chloroform:methanol:acetic acid (9:1:0.1) to obtain 3-Isopropyl-[(4-methyl-cyclohexanecarbonyl)-amino]-5m-tolyl-thiophene-2-carboxylic acid (15 mg, 52%) as a white solid. ^{1}H NMR (CDCl₃, 400 MHz): (s, 2H), 7.38 (t, 1H), 7.24 (m, 1H), 7.08 (s, 1H), 5.01 (s, 1H), 2.42 (s, 3H), 2.10-0.62 (m, 20H). ESI (M-H): 398.

Example 20

(1R, 2S, 4R) - 3 - [Isopropyl - (2-hydroxy - 4-methyl - 1)]

cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid Compound #402

(1R, 2S, 4R) -2-Hydroxy-4-methyl-cyclohexanecarboxylic acid methyl ester was prepared as described in J. Org. Chem, (1993), 58, pp.6255-6265. NMR ¹H (CDCl₃, 400 MHz): 4,26 ppm (s, 1H); 4,19-4,13 ppm (m, 2H); 3,16 ppm (s, 1H); 2,35-2,29 ppm (m, 1H); 1,92-1,74 ppm (m, 5H); 1,31-1,24 ppm (m, 3H); 1,08-1,01 ppm (m, 1H); 0,96-0,92 ppm (m, 1H); 0,88 ppm (d, 3H).

STEP I

5

To a solution of (1R,2S,4R)-2-Hydroxy-4-methyl-

cyclohexanecarboxylic acid methyl ester (450 mg, 2.42 mmol) in methanol (12 ml) was added a 2.5 M solution of sodium hydroxide (9.7 ml, 24.2 mmol). The reaction mixture was stirred for 4 h at 50 °C. Then, the solvents were removed and the residue was partitioned between 20 ml of H₂O acidified to pH 4 and 20 ml of EtOAc. The organic layer was separated and the aqueous phase was washed with ethyl acetate (2 X 20 ml). The combined ethyl acetate layers were dried (Na₂SO₄) and concentrated to obtain 313 mg (82 %) of (1R,2S,4R)-2-Hydroxy-4-methyl-cyclohexanecarboxylic

acid. NMR 1 H (CDCl₃, 400 MHz): 4,34 ppm (s, 1H); 2,43-2,39 ppm (m, 1H); 1,96-1,76 ppm (m, 5H); 1,14-1,08 ppm (m, 1H); 1,02-0,93 ppm (m, 1H); 0,90 ppm (d, 3H).

5 Step II

To a solution of (1R, 2S, 4R) -2-Hydroxy-4-methylcyclohexanecarboxylic acid (162 mg, 1.02 mmol) in dichloromethane (5 ml) was added pyridine (495 ul, 6.12 mmol) followed by acetic anhydride (385 ul, 4.08 mmol). The reaction 10 mixture was stirred for 20 h at room temperature. Then, the solvents were removed and 10 ml of 3N HCl solution was added. This mixture was stirred for 30 minutes and then a saturated solution of NaHCO3 was slowly added until pH = 9-10. This solution was then extracted with ethyl acetate (2 X 5 ml). The aqueous phase was then acidified with a 10% HCl solution and extracted with ethyl acetate (3X5 ml). The following ethyl acetate layers were combined, dried (Na2SO4) and concentrated to obtain 109 mg (53 %) of (1R,2S,4R)-2-Acetoxy-4-methylcyclohexanecarboxylic acid. NMR ¹H (CDCl₃, 400 MHz): 5,45 ppm (s, 1H); 2,46-2,42 ppm (m, 1H); 2,02 ppm (s, 3H); 2,02-1,96 ppm 20 (m, 1H); 1,91-1,76 ppm (m, 3H); 1,70-1,61 ppm (m, 1H); 1,16-1,08 ppm (m, 1H); 0,99-0,88 ppm (m, 1H); 0,87 ppm (d, 3H).

Step III

To a solution of (1R,2S,4R)-2-Acetoxy-4-methyl-cyclohexanecarboxylic acid (109 mg, 0.54 mmol) in dichloromethane (2.7 ml) was added oxalyl chloride (545 μl, 1.09 mmol) followed by 1 drop of dimethylformamide. The reaction mixture was stirred for 4 h at room temperature. The solvents were then removed to obtain 119 mg (99%) of (1R,2S,4R)-2-Acetoxy-4-methyl-cyclohexanecarboxylic acid chloride.

Step IV

To a solution of 3-Isopropylamino-5-phenyl-thiophene-2-carboxylic acid methyl ester (136 mg, 0.50 mmol) in 1,2-dichloroethane (1.0

ml) was added (1R,2S,4R)-2-Acetoxy-4-methyl-cyclohexanecarboxylic acid chloride (119 mg, 0.54 mmol) dissolved in 1,2-dichloroethane (0.6 ml) followed by PPh₃ (136 mg, 0.52 mmol). The resulting solution was stirred for 20 h at 90 °C and then cooled to room

- 5 temperature. It was then diluted with ethyl acetate (10 ml) and a solution of saturated NaHCO₃ (10 ml). The aqueous phase was separated and washed with ethyl acetate (2x10 ml) and the combined organic layers were dried (Na₂SO₄), filtered and concentrated. The residue was purified by flash chromatography (0% to 25%
- 10 EtOAc/Hexane) to obtain 110 mg (45%) of (1R,2S,4R)-3-[Isopropyl(2-Acetoxy-4-methyl-cyclohexanecarbonyl)-amino]-5-phenylthiophene-2-carboxylic acid methyl ester. NMR ¹H (CDCl₃, 400
 MHz): 1.5:1.0 mixture of rotamers 7,73-7,70 ppm (m, 2H, H_{aro});
 7,69-7,63 ppm (m, 1H, H_{aro}); 7,51-7,41 ppm (m, 4H, H_{aro}); 7,13 ppm
- 15 (s, 0.6H, H_{aro}, major rotamer); 5,79 ppm (s, 0.4H, minor rotamer);
 5,21 ppm (s, 0.6H, major rotamer); 4,95-4,88 ppm (m, 1H); 3,88 ppm
 (s, 1.8H, major rotamer); 3,87 ppm (s, 1.2H, minor rotamer); 2,402,36 ppm (m, 0.6H, major rotamer); 2.11 ppm (s, 3H); 1,78-0,77 ppm
 (m, 16H).

20

Step V

(1R,2S,4R)-3-[Isopropyl-(2-Acetoxy-4-methyl-cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic acid methyl ester (36 mg, 0.17 mmol) was dissolved in a mixture of

- dioxane: H_2O (4:1) (700 μ l) and then 470 μ l of LiOH 1N was added to it. After 3 h at 50 °C the reaction mixture was cooled to room temperature and the solvents were removed. The residue was then partitioned between 10 ml of H_2O acidified to pH 4 and 10 ml of EtOAc. The organic layer was separated and the aqueous phase was
- washed with ethyl acetate (2 X 10 ml). The combined ethyl acetate layers were dried (Na₂SO₄), concentrated and the residue was purified by preparative chromatography to obtain 9 mg (29 %) of (1R,2S,4R)-3-[Isopropyl-(2-hydroxy-4-methyl
 - cyclohexanecarbonyl)-amino]-5-phenyl-thiophene-2-carboxylic
- 35 acid. NMR ¹H (CDCl₃, 400 MHz): 3:2 mixture of rotamers 7,76-

7,73 ppm (m, 2H, H_{aro}); 7,50-7,38 ppm (m, 3H, H_{aro}); 7,36 ppm (s, 1H, H_{aro}); 4,93-4,87 ppm (m, 1H); 4,25 ppm (s, 0.70H, major rotamer); 3,97 ppm (s, 0.3H, minor rotamer); 2,35-2,28 ppm (m, 1H); 1,99=1,53 ppm (m, 5H); 1,28 ppm (d, 0,6H, minor rotamer); 5 1,25 ppm (d, 1,4H, major rotamer); 1,06-1,03 ppm (m, 3H), 0,96-0,72 ppm (m, 1H); 0,79 ppm (d, 3H); 0,67-0,56 ppm (m, 1H).

Example 21

3-[(2,4-Dichloro-benzoyl)-piperidin-4-yl-amino]-5-phenyl-10 thiophene-2-carboxylic acid hydrochloride salt compound #368

Step I

15 A suspension of 3-amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (745 mg, 3.2 mmol) in dry THF (1.3 ml), at 21 °C, under nitrogen, was treated with tert-butyl 4-oxo-1-piperidine carboxylate (673 mg, 3.2 mmol), followed by dibutyltin dichloride (19 mg, 0.064 mmol, 0.02 eq.). After 5 min the 20 reaction was treated with phenyl silane (435 μ L, 380 mg, 3.52 mmol, 1.1 eq). The mixture was left to stir for 74h when a clear solution resulted. The reaction was stripped off solvent to leave a thick bright yellow gum (1.59 g). The crude material was · purified by column chromatography using (CH2Cl2 : Hexane : EtOAc) 25 = 15 : 5 :1 as eluent to provide 4-(2-Methoxycarbonyl-5-phenyl-

thiophen-3-ylamino)-piperidine-1-carboxylic acid tert-butyl ester as a yellow foam (713 mg, 54%). ¹H NMR (CDCl₃, 400 MHz) 7.63-7.60 (m, 2H), 7.74-7.36 (m, 3H), 6.90-6.84 (bs, 1H), 6.84 (s, 1H), -3.97- 4.01 (m, 2H), 3.80 (s, 3H), 3.48 (bs, 1H), 3.06-5 2.99 (m, 2H), 2.03-1.99 (m, 2H), 1.51-1.48 (m, 2H), 1.47 (bs, 9H)

Step II

4-(2-Methoxycarbonyl-5-phenyl-thiophen-3-ylamino)-piperidine-110 carboxylic acid tert-butyl ester (200 mg, 0.48 mmol) was treated
 with 2,4 dichlorobenzoylchloride (202 μL, 302 mg, 1.44 mmol, 3 eq)
 under previously described conditions (e.g. Example 14) to
 provide, after column chromatography using (CH₂Cl₂: Hexane:
 EtOAc = 15:5:1) as eluent, 4-[(2,4-Dichloro-benzoyl)-(215 methoxycarbonyl-5-phenyl-thiophen-3-yl)-amino]-piperidine-1 carboxylic acid tert-butyl ester as a pale yellow foam (165 mg,
 58%), ¹H NMR (CDCl₃, 400 MHz) 7.54-7.51 (m, 2H), 7.45-7.39 (m,
 3H), 7.27-7.25 (m, 2H), 7.17 (d, J = 1.96Hz, 1H), 7.06 (dd, J =
 1.92Hz, J = 8.34Hz, 1H), 4.86-4.92 (m, 1H), 4.11-4.21 (m, 2H),
 3.89 (s, 3H), 2.82-2.89 (m, 2H), 2.17-2.20 (m, 1H), 1.89-1.92 (m,
 1H), 1.49-1.61 (m, 1H), 1.40 (bs, 9H), 1.19-1.25 (m, 1H)

Step III

A suspension of 4-[(2,4-Dichloro-benzoyl)-(2-methoxycarbonyl-5
phenyl-thiophen-3-yl)-amino]-piperidine-1-carboxylic acid tertbutyl ester (160 mg, 0.27 mmol) above in dioxane: water (4:1, 3

ml) was treated with lithium hydroxide (2M aqueous solution, 41

µL, 341 mg, 0.814 mmol, 3 eq) and the reaction allowed to stir

overnight for 18h. The reaction was stripped-off solvent and the

residue partitioned between EtOAc: water (4:1). The aqueous

phase was separated and extracted several times, with EtOAc,

following acidification to pH 5.5 with 0.1N HCl. The combined

organic extract was evaporated to a solid. The solid was taken

into EtOAc and the above acid wash repeated to give, after drying

and evaporation, 4-[(2-Carboxy-5-phenyl-thiophen-3-yl)-(2,4-

dichloro-benzoyl)-amino]-piperidine-1-carboxylic acid tert-butyl
 ester as a colourless solid (128 mg, 91%), ¹H NMR (Acetone, 400
 MHz) 7.75-7.70 (m, 1H), 7.64 (s, 1H), 7.52-7.40 (m, 3H), 7.52 (d,
 J = 1.98-Hz, 1H), 7.21 (dd, J = 1.96 Hz, J = 8.19 Hz, 1H), 4.805 4.71 (m, 1H), 4.26-4.01 (m, 2H), 2.71- 2.30 (bs, 3H), 2.25-2.17
 (m, 1H), 1.82-1.69 (m, 1H), 1.40 (bs, 9H), 1.33-1.24 (m, 1H).

Step IV

- A solution of 4-[(2-Carboxy-5-phenyl-thiophen-3-yl)-(2,4-dichloro-benzoyl)-amino]-piperidine-1-carboxylic acid tert-butyl ester (240 mg, 0.42 mmol) in dioxane (4 ml) at 21 °C under nitrogen was treated with anhydrous 4M HCl (3 ml, 12.6 mmol, 30 eq). After 4h the reaction was stripped off solvent and the residue triturated with ether to give 3-[(2,4-Dichloro-benzoyl)-piperidin-4-yl-amino]-5-phenyl-thiophene-2-carboxylic acid as a pale yellow
- powder (214 mg, 100 %) ¹H NMR (Acetone, 400 MHz) 7.76-7.73 (m, 2H), 7.64 (s, 1H), 7.45-7,38 (m, 3H), 7.30 (bs, 1H), 7.28-7.24 (m, 1H), 4.93-4.84 (m, 1H), 3.56-3.49 (m, 2H), 3.25-3.14 (m, 2H), 3.05-2.55 (bs, 1H), 2.50-2.37 (m, 2H), 2.13-1.83 (m, 1H).
- 20 Similarly prepared were Compound #366 , Compound #553 , Compound #543

Example 22

3-(Benzyl-cyclopropanecarbonyl-amino)-5-phenyl-thiophene-2-carboxylic acid. Compound #454

Step I

A solvent mixture of THF/MeOH/H₂O (3:2:1) was added to 3.04 g of methyl(3-amino-5-phenyl)thiophene-2-carboxylate (13 mmol) and 1.64 g of lithium hydroxide monohydrate (39 mmol). The mixture was refluxed for 8 hours and concentrated in vacuo. The crude material was taken in 100 ml of water, washed with ethyl acetate (2 x 100 ml) and transferred into a multineck flask. A 20% phosgene solution in toluene (11 ml, 39 mmol) was added dropwise at 0°C. A precipitate was then collected by filtration and sequentially washed by trituration with a saturated solution of bicarbonate, water, acetone and diethyl ether. 2.52 g (79%) of 6-phenyl-1H-thieno[3,2-d][1,3]oxazine-2,4-dione were isolated as a white solid. NMR ¹H (DMSO D₆, 400 MHz): 7.79-7.76 ppm (m, 2H, H_{aro}); 7.52-7.47 ppm (m, 3H, H_{aro}); 7.25 ppm (s, 1H, H_{azole}); 0.4 ppm (s, 1H, NH).

Step II

A solution of 6-phenyl-1H-thieno[3,2-d][1,3]oxazine-2,4-dione (1 g, 4.1 mmol) and anhydrous sodium carbonate (477 mg, 4.5 mmol) diluted in 15 ml of anhydrous dimethylacetamide was stirred for one hour under nitrogen before adding benzyl bromide (785 mg, 4.5 mmol). The mixture was stirred overnight at room temperature. 912 mg (66.3%) of 1-benzyl-6-phenyl-1H-thieno[3,2-

d][1,3]oxazine-2,4-dione were obtained as a pale yellow solid after filtration and washing the precipitate with acetone and pentane. NMR 1 H (DMSO D₆, 400 MHz): 7.8-7.76 ppm (m, 3H, H_{aro}); 7.51-7.45 ppm (m, 3H, H_{aro}); 7.43-7.41 ppm (m, 2H, H_{aro}); 7.35-7.3 5 ppm (m, 2H, H_{aro}); 7.28-7.24 ppm (m, 1H, H_{aro}); 5.22 ppm (s, 1H, NCH_2).

Step III

To a solution of 1-benzyl-6-phenyl-1H-thieno[3,2-d][1,3]oxazine-2,4-dione (880 mg, 2.62 mmol) were successively added 32 ml of dioxane and 7.87 ml of NaOH 1N aqueous solution. The mixture was vigourously stirred for 2 h and then the solvents were concentrated in vacuo. Dichloromethane was added to the crude material and sodium 3-benzylamino-5-phenyl-thiophene-2-15 carboxylate (1.07 g, 100%) precipitated as a pale yellow solid. NMR ¹H (DMSO D₆, 400 MHz): 7.76 ppm (t, 1H, J = 6.4 Hz, NH); 7.53-7.51 ppm (m, 2H, H_{aro}); 7.33-7.26 ppm (m, 6H, H_{aro}); 7.23-7.16 ppm (m, 2H, H_{aro}); 7.07 ppm (s, 1H, H_{azole}); 4.36 ppm (d, 2H, J = 6.4 Hz, NHCH₂).

20

35

Step IV

To a solution of sodium 3-benzylamino-5-phenyl-thiophene-2carboxylate (41.1 mg, 0.1 mmol) was added 32 mg (0.3 mmol) of cyclopropanecarbonyl chloride, 1.5 ml of dioxane and 0.5 ml of 25 water. The mixture was stirred overnight at room temperature and concentrated in vacuo. A 4N hydrogen chloride solution in dioxane (1 ml) was added and the mixture was stirred for one hour at room temperature. The mixture was again concentrated and the crude material was purified by reverse phase HPLC giving access to 11.9 mg (31.5%) of 3-(benzyl-cyclopropanecarbonylamino)-5-phenyl-thiophene-2-carboxylic acid as a pale yellow solid. NMR 1 H (DMSO D₆, 400 MHz): 7.56-7.54 ppm (m, 2H, H_{aro}); 7.39-7.13 ppm (m, 10H, H_{aro} , H_{azole} and COOH); 5.27 ppm (d, 1H, J =15.2 Hz); 4.48 ppm (d, 1H, J = 15.2 Hz); 1.49 ppm (m, 1H); 0.77 ppm (m, 2H); 0.61 ppm (m, 2H).

```
The following compounds were prepared in a similar manner:

Compound #172 , Compound #173 , Compound #175 , Compound #186 ,
Compound #187 , Compound #188 , Compound #241 , Compound #247 ,

Compound #251 , Compound #252 , Compound #253 , Compound #254 ,
Compound #255 , Compound #256 , Compound #257 , Compound #276 ,
Compound #277 , Compound #278 , Compound #279 , Compound #280 ,
Compound #281 , Compound #330 , Compound #334 , Compound #335 ,
Compound #336 , Compound #339 , Compound #340 , Compound #341 ,
Compound #342 , Compound #343 , Compound #344 , Compound #345 ,
Compound #347 , Compound #349 , Compound #350 , Compound #351 ,
Compound #384 , Compound #385 BCH-23932, Compound #354 ,
Compound #384 , Compound #385 , Compound #386 , Compound #388 ,
Compound #389 , Compound #390 , Compound #391 , Compound #392 ,
Compound #389 , Compound #394 , Compound #397 , Compound #398 ,
Compound #399 , Compound #394 , Compound #397 , Compound #398 ,
Compound #399 , Compound #400 , Compound #401 .
```

Example 23

3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-

20 thiophene-2-carboxylic acid

Step I

5 3-Iodo-5-phenyl-thiophene-2-carboxylic acid methyl ester

A suspension of 3-Amino-5-phenyl-thiophene-2-carboxylic acid methyl ester (10 g, 43 mmol) in anhydrous benzene (200 ml), at 21 °C, under N2, was treated with t-butyl nitrite (21.8 g, 86 mmol) and the dark mixture cooled to 0 °C and treated dropwise, over 15 min, with iodine (21.8 ml, 184 mmol). After 30 min at 0 °C, the solution was allowed to warm-up to ambient temperature and stirred for 2h. The reaction mixture was then poured into water (300 ml) and stirred vigorously for 15 min. The organic phase was separated and washed several times with 20% sodium thiosulfate (4x100 ml). The resulting emulsion was filtered through celite. The celite pad was washed with EtOAc and the combined filtrate and washings were washed with more sodium

thiosulfate (100 ml) to give an orange solution which was washed wth brine and dried. Evaporation of the solvent afforded an oil (7.4 g). The crude oil was purified by biotage flash chromatography using Hexane/CH₂Cl₂/EtOAc (20/2/1) as eluent to give 4.42g (29%) of 3-Iodo-5-phenyl-thiophene-2-carboxylic acid methyl ester as a pale yellow oil. NMR ¹H (CDCl₃, 400 MHz,): 7.62-7.57 (m, 2H); 7.58 (s, 1H); 7.50-7.36 (m, 3H); 3.91 (s, 3H)

Step II

10 3-Iodo-5-phenyl-thiophene-2-carboxylic acid

A solution of 3-Iodo-5-phenyl-thiophene-2-carboxylic acid methyl ester (4.4 g, 12.78 mmol) in dioxane/water 4/1 (50 ml), at 21 °C, under N₂, was treated with lithium hydroxyde (2N, 19.3 ml, 38 mmol) and the solution left to stir for 21.5 h. The reaction mixture was evaporated to dryness and the residue partitioned between EtOAc (75 ml) and water (25 ml) and acidified with 2N HCl to pH 5.5. The aqueous phase was separated and extracted with EtOAc (3x50 ml). The combined organic extract were washed with brine, dried and evaporated to give 4.12 g (97%) of 3-Iodo-5-phenyl-thiophene-2-carboxylic acid as a pale yellow solid. NMR ¹H (CD₃OD, 400 MHz): 7.69-7.67 (m, 2H); 7.55 (s, 1H); 7.46-7.39 (m, 3H).

25 Step III

3-Iodo-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester

A suspension of magnesium sulfate (4.61 g, 38.32 mmol) in dichloromethane (37 ml) at 21 °C, under N₂, was treated with conc H₂SO₄ (510 μl, 9.58 mmol). After 15 min solid 3-Iodo-5-phenyl-thiophene-2-carboxylic acid (3.7 g, 9.58 mmol) was added followed by t-butanol (4.55 ml, 47.9 mmol) and the flask was stoppered and left over-night for 19.5 h. The reaction mixture was treated with saturated bicarbonate aqueous solution, and filtered. The solid was washed with CH₂Cl₂ and the filtrate dried

and concentrated to an oil. The crude material was purified by flash chromatography using Hexane/CH₂Cl₂ (3:1) as eluent to give 1,63 g (44%) of 3-Iodo-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester as a colorless solid. NMR ¹H (CDCl₃, 400 MHz) 7.61-7.59 (m, 2H); 7.43-7.35 (m, 3H), 7.25 (s, 1H), 1.60 (bs, 9H).

Step IV

10

3-Formyl-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester

A solution of 3-Iodo-5-phenyl-thiophene-2-carboxylic acid tertbutyl ester (1.41 g, 3.65 mmol) in dry THF (37 ml) at -78°C, under nitrogen, was treated dropwise, over 5 min with n-butyl lithium (4.8 ml, 7.66 mmol). The reaction gradually darkened to a red-brown color. After 15 min at -78 °C dimethylformamide (1.7 ml, 21.9 mmol) was added dropwise over 7 min. The dark solution was allowed to stirr for 2 h then quenched with saturated NH₄Cl solution (10 ml) and allowed to reach 21°C. The aqueous phase was separated and extracted with EtOAc (3x50 ml). The combined organic extracts were evaporated and the residue taken into EtOAc and washed with water, brine, dried and concentrated to give 1.14 g of a brownn oil. The crude material was purified by

provide 303 mg (28%) of 3-Formyl-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester as a colorless solid. NMR ¹H: (CDCl₃, 400 MHz): 10.62 (s, 1H); 7.78 (s, 1H); 7.64-7.62 (m, 2H); 7.48-7.38 (m, 3H); 1.62 (bs, 9H).

flash chromatography using Hexane/CH2Cl2 (1/1) as eluent to

Step V

30 5-Phenyl-thiophene-2,3-dicarboxylic acid 2-tert-butyl ester

A solution of 3-Formyl-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester (300 mg, 1.04 mmol) in dry THF (20 ml), at 0 °C, under nitrogen, was treated with methyl sulfide (10% w/w in THF,

35 3.8 ml, 5.2 mmol) followed by sodium dihydrogenphosphate (30%

aqueous solution , 9.56 ml, 2.05 mmol). After 0.5 h, the solution was treated with sodium chlorite (30% w/w aqueous solution, 1.9 ml, 2.08 mmol) added over 1 min via a syringe. The pale yelfow solution was stirred for 1.5 h at 0 °C, then diluted with water (20 ml) and extracted with EtOAc (4x 40 ml). The aqueous phase was separated, extracted with more EtOAc (40 ml) and the combined extracts were washed with brine dried and concentrated to give 316 mg (100 %) of 5-Phenyl-thiophene-2,3-dicarboxylic acid 2-tert-butyl ester as a pale brown solid. NMR of 1 (CD3CO; 400 MHz): 7.87 (s, 1H); 7.83-7.81 (m, 2H); 7.17-7.53 (m, 3H); 1.65 (bs, 9H).

Step VI

3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-15 thiophene-2-carboxylic acid tert-butyl ester

A solution of 5-Phenyl-thiophene-2,3-dicarboxylic acid 2-tertbutyl ester (40 mg, 0.13 mmol) in CH₂Cl₂ (1.3 ml), under nitrogen, at 0° C, was treated with diisopropylethylamine (27 \square L, 20 0.16 mmol) followed by dimethylformamide (10 \square L, 0.13 mmol) and oxalyl chloride (170 L, 0.34 mmol). Slight effervescence was observed. The reaction was kept at 0 °C for 30 min before being treated with (2,4-Dichloro-phenyl)-isopropyl-amine (described previously) (79 mg, 0.39 mmol). The reaction was allowed to 25 reach 21 °C and then placed in a bath at 90 °C for 15 h. Solvent was removed to leave a pale brown gum (144 mg). The crude material was purified on bond-elute using Hexane/CH2Cl2/EtOAc (12.5/2/1) as eluent to give 39 mg, (62%) of 3-[(2,4-Dichlorophenyl)-isopropyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid tert-butyl ester as a pale brown solid. NMR 1H (CDCl3; 400 MHz) 7.50-7.48 (m, 2H); 7.38-7.25 (m, 6H); 7.10-7.03 (m, 1H); 5.05 (quint, J = 6.88 Hz, 1H); 1.57 (bs, 9H); 1.40 (d, J = 6.88)Hz, 3H); 1.12 (d, J = 6.88 Hz, 3H)

³⁵ Step VII

3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid

A solution of 3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5
5 phenyl-thiophene-2-carboxylic acid tert-butyl ester (37 mg, 0.08 mmol) in CH₂Cl₂ (0.2 ml) at room temperature, under nitrogen was treated with trifluoroacetic acid (0.8 ml). After 1 h the reaction was concentrated the residue was taken into EtOAc and washed sequentially with 2N HCl (2x15 ml), water, brine dried and evaporated to a foam (33 mg). The foam was redissolved in EtOAc and above acidic wash was repeated to yield 27 mg (84 %) of 3-[(2,4-Dichloro-phenyl)-isopropyl-carbamoyl]-5-phenyl-thiophene-2-carboxylic acid compound as pale brown foam. NMR ¹H: (CD₃OD; 400 MHz) 7.57-7.55 (m, 2H); 7.49-7.36 (m, 6H), 7.30-15 7.27 (m, 1H); 4.89 (quint, J = 6.73 Hz, 1H); 1.42 (d, J = 6.73 Hz, 3H); 1.12 (d, J = 6.73 Hz, 3H).

Example 24 The following compound was obtained from Discovery Technology:

3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-phenyl-thiophene-2-carboxylic acid amide Compound #580

Example 25 The following compounds were obtained from Maybridge:
5-(4-Chloro-phenyl)-3-(toluene-4-sulfonylamino)-thiophene-225 carboxylic acid amide, Compound #563
5-(4-Fluoro-phenyl)-3-(toluene-4-sulfonylamino)-thiophene-2carboxylic acid amide, Compound #564, GK 01137
5-(4-Methoxy-phenyl)-3-(toluene-4-sulfonylamino)-thiophene-2carboxylic acid amide, Compound #565, GK 01175

Example 26 Evaluation of compounds in The HCV RNA-Dependent RNA Polymerase Assay

The following references are all incorporated by reference:

1. Behrens, S., Tomei, L., De Francesco, R. (1996) EMBO 15, 12
22

Harlow, E, and Lane, D. (1988) Antibodies: A Laboratory
 Manual. Cold Spring Harbord Laboratory. Cold Spring Harbord.
 NY.

- 3. Lohmann, V., Körner, F., Herian, U., and Bartenschlager, R. (1997) *J. Virol.* 71, 8416-8428
- 4. Tomei, L., Failla, C., Santolini, E., De Francesco, R., and La Monica, N. (1993) J Virol 67, 4017-4026

Compounds were evaluated using an *in vitro* polymerase assay

10 containing purified recombinant HCV RNA-dependent RNA polymerase

(NS5B protein). HCV NS5B was expressed in insect cells using a
recombinant baculovirus as vector. The experimental procedures
used for the cloning, expression and purification of the HCV

NS5B protein are described below. Follows, are details of the

15 RNA-dependent RNA polymerase assays used to test the compounds.

Expression of the HCV NS5B protein in insect cells:

The cDNA encoding the entire NS5B protein of HCV-Bk strain, genotype 1b, was amplified by PCR using the primers NS5Nhe5'

- 20 (5'-GCTAGCGCTCAATGTCCTACACATGG-3') and XhoNS53' (5'CTCGAGCTCGAGCGTCCATCGGTTGGGGAG-3') and the plasmid pCD 3.8-9.4
 as template (Tomei et al, 1993). NS5Nhe5' and XhoNS53' contain
 two NheI and XhoI sites (underlined sequences), respectively, at
 their 5' end. The amplified DNA fragment was cloned in the
- 25 bacterial expression plasmid pET-21b (Novagen) between the restriction sites NheI and XhoI, to generate the plasmid pET/NS5B. This plasmid was later used as template to PCRamplify the NS5B coding region, using the primers NS5B-H9 (5'-ATACATATGGCTAGCATGTCCTACACATGG-3') and NS5B-R4 (5'-
- GGATCCGGATCCCGTTCATCGGTTGGGGAG-3'). NS5B-H9 spans a region of 15 nucleotides in the plasmid pET-21b followed by the translation initiation codon (ATG) and 8 nucleotides corresponding to the 5' end of the NS5B coding region (nt. 7590-7607 in the HCV sequence with the accession number M58335).
- NS5B-R4 contains two BamHI sites (underlined) followed by 18 nucleotides corresponding to the region around the stop codon in the HCV genome (nt. 9365-9347). The amplified sequence, of 1.8 kb, was digested with NheI and BamHI and ligated to a predigested pBlueBacII plasmid (Invitrogen). The resulting
- 40 recombinant plasmid was designated pBac/NS5B. Sf9 cells were

co-transfected with 3 μg of pBac/NS5B, together with 1 μg of
linearized baculovirus DNA (Invitrogen), as described in the
manufacturer's protocol. Following two rounds of plaque
purification, an NS5B-recombinant baculovirus, BacNS5B, was

isolated. The presence of the recombinant NS5B protein was
determined by western blot analysis (Harlow and Lane, 1988) of
BacNS5B-infected Sf9 cells, using a rabbit polyclonal antiserum
(anti-NS5B) raised against a His-tagged version of the NS5B
protein expressed in E. coli. Infections of Sf9 cells with this
plaque purified virus were performed in one-liter spinner flasks
at a cell density of 1.2 x 10⁶ cells/ml and a multiplicity of
infection of 5.

Preparation of a soluble recombinant NS5B protein

15 Sf9 cells were infected as described above. Sixty hours post-infection, cells were harvested then washed twice with phosphate buffer saline (PBS). Total proteins were solubilized as described in Lohmann et al. (1997) with some modifications. In brief, proteins were extracted in three steps, S1, S2, S3, using lysis buffers (LB) I, LB II and LB III (Lohmann et al, 1997). The composition of LBII was modified to contain 0.1 % triton X-100 and 150 mM NaCl to reduce the amount of solubilized NS5B protein at this step. In addition, sonication of cell extracts was avoided throughout the protocol to preserve the integrity of the protein structure.

Purification of recombinant NS5B using fast protein liquid chromatography (FPLC):

Soluble NS5B protein in the S3 fraction was diluted to lower the NaCl concentration to 300 mM, then it incubated batchwise with DEAE sepharose beads (Amersham-Pharmacia) for 2 hrs at 4°C, as described by Behrens et al. (1996). Unbound material was cleared by centrifugation for 15 min at 4°C, at 25 000 rpm using a SW41 rotor (Beckman). The supernatant was further diluted to lower the NaCl concentration to 200 mM and subsequently loaded, with a flow rate of 1 ml/min, on a 5 ml HiTrap® heparin column (Amersham-Pharmacia) connected to an FPLC® system (Amersham-Pharmacia). Bound proteins were eluted in 1 ml fractions, using a continuous NaCl gradient of 0.2 to 1 M, over a 25 ml volume.

WO 02/100851 PCT/CA02/00876 NS5B-containing fractions were identified by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), followed by western blotting using the anti-NS5B antiserum at a dilution of 1:2000. Positive fractions were pooled and the elution 5 buffer was exchanged against a 50 mM NaPO, pH 7.0, 20 % glycerol, 0.5 % triton X-100 and 10 mM DTT, using a PD-10 column (Amersham-Pharmacia). The sample was then loaded onto a 1 ml HiTrap® SP column (Amersham-Pharmacia), with a flow rate of 0.1 ml/min. Bound proteins were eluted using a continuous 0 to 1 M 10 NaCl gradient over a 15 ml volume. Eluted fractions were analyzed by SDS-PAGE and western blotting. Alternatively, proteins were visualized, following SDS-PAGE, by silver staining using the Silver Stain Plus kit (BioRad) as described by the manufacturer. Positive fractions were tested for RdRp activity 15 (see below) and the most active ones were pooled, and stored as a 40 % glycerol solution at -70°C.

In vitro HCV RdRp Flashplate scintillation proximity assay (STREP-FLASH ASSAY) used to evaluate analogues:

20 This assay consists on measuring the incorporation of [3H] radiolabelled UTP in a polyrA/ biotinylated-oligo dT templateprimer, captured on the surface of streptavidin-coated scintillant-embeded microtiter Flashplates (NEN Life Science 25 Products inc, MA, USA, SMP 103A). In brief, a 400 ng/ul polyrA solution (Amersham Pharmacia Biotech) was mixed volume-to-volume with 5' biotin-oligo dT_{15} at 20 pmol/ μ l. The template and primers were denatured at 95 C for 5 minutes then incubated at 37 C for 10 minutes. Annealed template-primers were 30 subsequently diluted in a Tris-HCl containing buffer and allowed to bind to streptavidin-coated flashplates overnight. Unbound material was discarded, compounds were added in a 10 μl solution followed by a 10 µl of a solution containing 50 mM MgCl,, 100 mM Tris-HCl pH 7.5, 250 mM NaCl and 5 mM DTT. The enzymatic reaction was initiated upon addition of a 30 µl solution containing the enzyme and substrate to obtain the following concentrations: 25 µM UTP, 1 µCi [3H] UTP and 100 nM recombinant HCV NS5B. RdRp reactions were allowed to proceed for 2 hrs at room temperature after which wells were washed three times with 40 a 250μL of 0.15 M NaCl solution, air dried at 37 C, and counted

WO 02/100851 PCT/CA02/00876 using a liquid scintillation counter (Wallac Microbeta Trilex, Perkin-Elmer, MA, USA). Results are shown in Table 1.

In vitro HCV RdRp filtration assay used to evaluate analogues 5 RdRp assays were conducted using the homopolymeric template/primer polyA/oligo dT. All RdRp reactions were performed in a total volume of 50 µl, and in a basic buffer consisting of 20 mM Tris-HCl pH 7.5, 1mM DTT, 50 mM NaCl, 5 mM MgCl₂, 0.5 μ Ci [γ^{32} P]-UTP (3000 Ci/mmol), 15 μ M cold UTP and 20 U 10 RNasin (Promega). Standard HCV RdRp reactions contained 200 ng of purified NS5B protein. PolyA RNAs (Amersham-Pharmacia) was resuspended at 400 ng/µl. The primer oligodT, (Canadian life technologies) was diluted to a concentration of 20 pmol/ μ l (7.6 ng/ml). Templates and primers were mixed volume to volume, 15 denatured at 95°C for 5 min and annealed at 37°C for 10 min. Following a two hour incubation at 22°C, reactions were stopped by the addition of 100 µg of sonicated salmon sperm DNA (Life Technologies) and 1 ml of 10 % trichloroacetic acid-0.5 % tetrasodium pyrophosphate (TCA-PPi). Nucleic acids were 20 precipitated at 4°C for 30 min after which samples were filtered on GF/C glass microfiber filters (Millipore). Membranes were subsequently washed with 25 ml of a 1% TCA-0.1 % PPi solution, then air dried. Incorporated radioactivity was quantified using a liquid scintillation counter (1450-Microbeta, Wallac). Results 25 are shown in Table 1.

Example 27 Evaluation of Analogues for measurement of ATPase activity of HCV NS3 helicase

30 Malachite Green Assay:

The measurement of ATPase activity was performed by measuring the amount of free inorganic phosphate released during the conversion of ATP to ADP by the HCV NS3 ATPase activity. The assay is as follows: In a 96-well microtiter-plate, compounds were dissolved at various concentrations in a final volume of 25 µL of ATPase buffer containing 400 µM ATP. The enzymatic

reaction was initiated by the addition of 25 μ l of ATPase buffer containing 6 nM of HCV NS3 enzyme without ATP to the wells followed by an incubation of 30 min. at 37 C. Essentially, the final concentration of the ATPase buffer components are as 5 follows: 44 mM MOPS pH 7.0, 8.8 mM NaCl, 2.2 mM MqCl, 125 μq/ml poly A, 1% DMSO, 200 µM ATP, and 3 nM HCV NS3 enzyme. reaction was stopped by the addition of 100 µl of Biomol Green™ reagent (BIOMOL® Research Laboratories Inc., Plymouth Meeting, In order to allow the development of the green color, the plate was incubated for 15 min. at room temperature. plate was read on a micro-plate reader at 620 nm. inhibitory concentration (IC_{so}) for anti-ATPase activity was defined as the concentration of compound that resulted in a 50 % reduction of the signal compared to the signal observed in control sample without compound. The signal recorded was also 15 corrected from the background signal obtained with control samples with compound only. The IC, was determined from doseresponse curves using six to eight concentrations per compound. Curves were fitted to data points using a non-linear regression analysis, and IC_{50} s were interpolated from the resulting curves using GraphPad Prism software, version 2.0 (GraphPad Software Inc, San Diego, CA).

HPLC Assay:

25

The measurement of HCV NS3 ATPase activity was performed by measuring the amount of ADP produced during the conversion of ATP to ADP by the HCV NS3 enzyme using paired-ion HPLC on a reverse phase column. The assay is as follows: The same protocol as mentioned above was used except that the final concentration of HCV NS3 enzyme was reduced to 1 nM in a 50 μl reaction mixture and that the ATPase reaction was stopped by the addition of 12.5 μl of 0.5 M EDTA. A modular liquid chromatography system (TSP Spectrasystem®, ThermoQuest

Corporation, San Diego, USA) using a ChromQuest[™] software (ThermoQuest Corporation, San Diego, USA) controlled the autosampling of 25 μl from each reaction. The mobile phase was

an isocratic solution of 0.15 M triethylamine, 6% methanol, and phosphoric acid to pH 5.5. ADP and ATP peaks were resolved using the Aqua 5 $\mu,$ C18, 125 Å, (150 X 4.6 mm) reverse phase column. The extent of ATP conversion to ADP was evaluated by 5 measuring the area under the ADP peak produced which was detected at 259 nm. The amount of ADP was corrected for the presence of ADP contaminant in the original ATP solution. 50% inhibitory concentration (IC₅₀) for anti-ATPase activity was defined as the concentration of compound that resulted in a 50 % 10 reduction of the ADP peak area compared to the ADP peak area observed in control sample without compound. The IC, was determined from dose-response curves using six to eight concentrations per compound. Curves were fitted to data points using a non-linear regression analysis, and $IC_{50}s$ were 15 interpolated from the resulting curves using GraphPad Prism software, version 2.0 (GraphPad Software Inc, San Diego, CA).

EXAMPLE 27 List of compounds and related polymerase activity *

	MOLSTRUCTURE	COMPOUND NAME	IC50
1		3-[(4-CHLORO-2,5-DIMETHYL- BENZENESULFONYL)-(3-IODO-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	
2	CI CH ₃ O O O O H	3-{(3-BENZOFURAN-2-YL-BENZYL)-(4- CHLORO-2,5-DIMETHYL- BENZENESULFONYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
. 3	CI H ₃ C CH ₃ O _{HN} OOH	3-(4-CHLORO-2,5-DIMETHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
4	F F O O O O O O O O O O O O O O O O O O	3-{(2,4-DICHLORO-BENZOYL)-[5-(3- TRIFLUOROMETHYL-PHENYL)-FURAN-2- YLMETHYL]-AMINO}-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++

L	 MOLSTRUCTURE	COMPOUND NAME	IC50
5	H ₃ C CH ₃ CH ₃ OH	3-[(4-CHLORO-2,5-DIMETHYL- BENZENESULFONYL)-METHYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
6	CH ₃ O. S O	5-(4-FLUORO-PHENYL)-3-(TOLUENE-4- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
7	CI CI SI-S=O	3-(2,4-DICHLORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
8	H ₃ C CH ₃ H O CH ₃ CH ₃	3-(4-CHLORO-2,5-DIMETHYL- BENZENESULFONYLAMINO)-5-(4- FLUORO-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	+++
9	ОН	3-[(2,4-DICHLORO-BENZOYL)-METHYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
10	CI OSPO NH H3C CH3/SOH H3C O	5-#TERT!-BUTYL-3-(4-CHLORO- BENZENESULFONYLAMINO)-	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
11	H,C OS ON OH	4-(TOLUENE-4-SULFONYLAMINO)- [2,3]BITHIOPHENYL-5-CARBOXYLIC ACID	++
12	S OH	3-[(5-BENZOFURAN-2-YL-THIOPHEN-2- YLMETHYL)-(2,4-DICHLORO-BENZOYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
13	CH,	5-PHENYL-3-(TOLUENE-4- SULFONYLAMINO)-THIOPHENE-2-	
14	H ₃ C CI H ₀ C CH ₃	3-(4-CHLORO-2,5-DIMETHYL- BENZENESULFONYLAMINO)-5-(4- CHLORO-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	+++
15		5-PHENYL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+

	MOLSTRUCTURE	COMPOUND NAME	IC50
16	CH ₃ O=S.NH OH	5-PHENYL-3-(TOLUENE-3- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++
17	HN S	3-BENZENESULFONYLAMINO-5-PHENYL-	++
18	HOS CI	3-(4-CHLORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
19	H.C S ED.H	3-(4-CHLORO-2,5-DIMETHYL- BENZENESULFONYLAMINO)-5-(4- ISOBUTYL-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	++
20	0.3	5-TERT-BUTYL-3-(4-CHLORO-2,5- DIMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	++
21		3-(2,5-DIMETHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	

		MOLSTRUCTURE	COMPOUND NAME	IC50
2	22	H ₃ C O-CH ₃ H ₃ C O-CH ₃	3-(4-METHOXY-2,3,6-TRIMETHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
2	3	. 🍑	5-PHENYL-3-(THIOPHENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
2	4	S	4-(4-CHLORO-2,5-DIMETHYL- BENZENESULFONYLAMINO)- [2,3"]BITHIOPHENYL-5-CARBOXYLIC ACID	+++
2	5	F ∕ F .	5-(3,5-BIS-TRIFLUOROMETHYL-PHENYL)- 3-(4-CHLORO-2,5-DIMETHYL- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	•
20	6	S EQ₂H	8-CHLORO-3-(4-CHLORO-2,5-DIMETHYL- BENZENESULFONYLAMINO)-4#H!-1,5- DITHIA- CYCLOPENTA[#A!]NAPHTHALENE-2- CARBOXYLIC ACID	++
27	7		3-(2,4-DIFLUORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
28	CI ON NH OH	3-[3-(2,6-DICHLORO-PYRIDIN-4-YL)- UREIDO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
29	N-S-OH CI	3-(2-CHLORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
30	S OH	3-(2-FLUORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+ +
31	S OH FF	5-PHENYL-3-(2-TRIFLUOROMETHOXY- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+
32	H ₃ C _C CH ₃ CCH ₃ OOH	3-(4-#TERT!-BUTYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
33	S.	3-(4-CHLORO- PHENOXYCARBONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	· +

	MOLSTRUCTURE	COMPOUND NAME	IC50
34	The state of the s	3-(3,4-DICHLORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
35	F O= SOOH	5-PHENYL-3-(2-TRIFLUOROMETHYL- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+
36		3-(5-BROMO-6-CHLORO-PYRIDINE-3- SULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+
37	~	3-(5-CHLORO-THIOPHENE-2- SULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
38	CH, CH, SHOOH	3-(5-CHLORO-3-METHYL- BENZO[#BI]THIOPHENE-2- SULFONYLAMINO)-5-PHENYL-	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
39	Br-S-20 NH 	3-(4-BROMO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
40	CI O=S.NH OH	3-(3-CHLORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
41	H ₃ C O O O O O O O O O O O O O O O O O O O	3-(5-CHLORO-1,3-DIMETHYL-1#H!- PYRAZOLE-4-SULFONYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
42	HO.S Br	3-(3-BROMO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
43		3-(4-ISOPROPYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
44	~	3-(2,6-DICHLORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	-+-

	MOLSTRUCTURE	COMPOUND NAME	IC50
45	O NH OH	3-(2-NITRO-BENZENESULFONYLAMINO)- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
46	N-S S O NH OH	5-PHENYL-3-(5-[1,2,3]THIADIAZOL-4-YL- THIOPHENE-2-SULFONYLAMINO)-	
47	N-O O=S.NH - S OH	5-PHENYL-3-(PYRIDINE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	
48	CI NH S OH	3-(2,4-DICHLORO-BENZYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
19	F O O O O O O O O O O O O O O O O O O O	3-(3-FLUORO- BENZENESULFONYLAMINO)-5-PHENYL-	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
	F F O O O O	,	
50	он .	5-PHENYL-3-(3-TRIFLUOROMETHYL- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	++
51	HOH OCH,	3-(2-CARBOXY-BENZOYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID METHYL ESTER	
52	J-S-OH FF	5-PHENYL-3-(4-TRIFLUOROMETHYL- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
53	H-SiOH F	3-(2,5-DIFLUORO- BENZENESULFONYLAMINO)-5-PHENYL-	+++
54	O S S NH O OH	3-(2-CYANO- BENZENESULFONYLAMINO)-5-PHENYL-	+++
55	CI O=S, NH	3-(2,5-DICHLORO-THIOPHENE-3- SULFONYLAMINO)-5-PHENYL-	,

	MOLSTRUCTURE	COMPOUND NAME	IC50
		I Sens Control (Galle	1030
56	S OH CH,	4-(TOLUENE-2-SULFONYLAMINO)- [2,2]BITHIOPHENYL-5-CARBOXYLIC ACID	+++
57	CAN SOUTH	5'-CHLORO-4-(TOLUENE-2- SULFONYLAMINO)-[2,2']BITHIOPHENYL-5- CARBOXYLIC ACID	+++
58	CI S OH CH3	5-(2,4-DICHLORO-PHENYL)-3-(TOLUENE- 2-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+ +
59	o-N-S-OH-CH3	5-(4-NITRO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
60	FFOOH SHOOT	3-(TOLUENE-2-SULFONYLAMINO)-5-(4- TRIFLUOROMETHOXY-PHENYL)-	- ++
61	N N-S O CH,	5-QUINOLIN-8-YL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	-
62		5-PHENYL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
63	O-N.O	5-(3-NITRO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	
64	H ₋ S OH CH,	3-(TOLUENE-2-SULFONYLAMINO)-5-M- TOLYL-THIOPHENE-2-CARBOXYLIC ACID	
65	H-SOCH ₃	5-(3-CHLORO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
66	F S OH CH,	5-(4-FLUORO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2-	+++
67	HOCH, SOHOH	5-(3-FLUORO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
68		5-(4-CHLORO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	PCT/CA02/00
 		COMPOSIND NAME	IC50
69	F S OH CH,	5-(3,5-DIFLUORO-PHENYL)-3-(TOLUENE- 2-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
70	F S O CHS	5-(3,4-DIFLUORO-PHENYL)-3-(TOLUENE- 2-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
71	H ₂ C SOH CH ₃	3-(TOLUENE-2-SULFONYLAMINO)-5- VINYL-THIOPHENE-2-CARBOXYLIC ACID	++
72	ONH NH OH	3-(4-CHLORO-BENZOYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
73	N-CH ₃ .	3-[(4-CHLORO-BENZOYL)-METHYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
74	O S NH	5-PHENYL-3-[(THIOPHENE-2- CARBONYL)-AMINO]-THIOPHENE-2- CARBOXYLIC ACID	-+

	MOLSTRUCTURE	COMPOUND NAME	IC50
75	O S N-CH ₃	3-[METHYL-(THIOPHENE-2-CARBONYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
76	Br O=S.NH	3-(2-BROMO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
77	S OH	3-(2,4-DIFLUORO-BENZOYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
78		3-[(2,4-DIFLUORO-BENZOYL)-METHYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	
79		3-(TOLUENE-2-SULFONYLAMINO)-5- TRIMETHYLSILANYLETHYNYL- THIOPHENE-2-CARBOXYLIC ACID	+++
80	0	5-ETHYNYL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
81	F O CH	3-(TOLUENE-2-SULFONYLAMINO)-5-(3- TRIFLUOROMETHOXY-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	
82	H-S OH CH,	5-BENZOYL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++
83	N C N C N C N C N C N C N C N C N C N C	5-(4-CYANO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
84	CI F	5-(3-CHLORO-4-FLUORO-PHENYL)-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
85	CI CI CI CH,	5-(3,4-DICHLORO-PHENYL)-3-(TOLUENE- 2-SULFONYLAMINO)-THIOPHENE-2-	++
86		5-PYRIDIN-4-YL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
87	HO O	5-PYRIDIN-3-YL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
. 88	HO O CH ₃	3-(TOLUENE-2-SULFONYLAMINO)-5-(4- TRIFLUOROMETHYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	+++
89	H,C S HO O CH,	5-(4-METHANESULFONYL-PHENYL)-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
90	H,C HOO CH,	5-(3-ACETYLAMINO-PHENYL)-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	++
91	F CI	5-(3-CHLORO-4-FLUORO-PHENYL)-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	++
92		3-(4-METHYL-BENZOYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC	++
93	OH CH ₃	3-[METHYL-(4-METHYL-BENZOYL)- AMINO]-5-PHENYL-THIOPHENE-2-	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
94	H,C OS OH	3-(3,5-DIMETHYL-ISOXAZOLE-4- SULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
95	N-CH, OH	3-[(2-CHLORO-BENZOYL)-METHYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
96	O NH CH ₃	3-(2-METHYL-BENZOYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
97	O CH ₃ N-CH ₃ OH	3-[METHYL-(2-METHYL-BENZOYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	·
98	0	5-PHENYL-3-(5-TRIFLUOROMETHYL- PYRIDINE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	++
99)	5-PHENYLETHYNYL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	

	MOLSTRUCTURE	COMPOUND NAME	IC50
		JOHN GOND HAME	1030
100	CH ₃ CO=S, NH OH SOON	3-(2,5-DIMETHYL- BENZENESULFONYLAMINO)-5-(4-NITRO- PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
101	CH _s O=s, NH OH	5-(2-FLUORO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
102	CH, O=S,NH OH	5-(2-CYANO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++
103	H ₃ C CH ₃ O NH O NH O OH	5-(2-ETHOXYCARBONYL-PHENYL)-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	++
104	O=S, NH O-CH, NH OH	5-(2-METHOXY-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2-	

	MOLSTRUCTURE	COMPOUND NAME	IC50
105	CH ₃ O=S, OH CH ₃ OH OH	3'-METHYL-4-(TOLUENE-2- SULFONYLAMINO)-[2,2']BITHIOPHENYL-5- CARBOXYLIC ACID	++
106	CH _s O=s OH OH	3-(TOLUENE-2-SULFONYLAMINO)-5-(2- TRIFLUOROMETHYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	++
107	FOR CH ₃	3-(2,5-DIMETHYL- BENZENESULFONYLAMINO)-5-(4- FLUORO-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	+++
108	S OH CH3	5-STYRYL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	· · ·
109	0	3-(2,4-DIFLUORO- BENZENESULFONYLAMINO)-5-(4-NITRO- PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	
110	FOH SOH	3-(2,4-DIFLUORO- BENZENESULFONYLAMINO)-5-(4- FLUORO-PHENYL)-THIOPHENE-2-	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
111	a Ja	3-[[5-(3-CHLORO-4-FLUORO-PHENYL)- THIOPHEN-2-YLMETHYL]-(2,4- DICHLORO-BENZOYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
112	S OH	3-[(4-OXO-1-PHENYL-1,3,8-TRIAZA- SPIRO[4.5]DECANE-8-CARBONYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
113	S T OH	3-{[4-(2-OXO-2,3-DIHYDRO- BENZOIMIDAZOL-1-YL)-PIPERIDINE-1- CARBONYL]-AMINO}-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	-
114	O NH O NH O OH	3-{[4-(4-NITRO-PHENYL)-PIPERAZINE-1- CARBONYL]-AMINO}-5-PHENYL-	+++
115		5-(2-CARBOXY-PHENYL)-3-(TOLUENE-2- BULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
			1030
116	H S OH	5-(4-CHLORO-PHENYL)-3-(PYRIDINE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	
117	S OH	5-(3-CYANO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	
 	ЧС .	·	+++
118	н,с	3-(2,5-DIMETHYL- BENZENESULFONYLAMINO)-5-P-TOLYL- THIOPHENE-2-CARBOXYLIC ACID	+++
119	H ₃ C OH	3-(2,4-DIFLUORO- BENZENESULFONYLAMINO)-5-P-TOLYL- THIOPHENE-2-CARBOXYLIC ACID	+++
120		5-PHENETHYL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2-	
	S OH		
121	сн,	5-(3-ETHOXYCARBONYL-PHENYL)-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
\		COMPOUND MAINE	1050
122	H _s C. OH	5-(4-METHOXY-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
123	CH ₃ S OH	5-(3-METHOXY-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
124	в в в в в в в в в в в в в в в в в в в	5-(4'-BROMO-BIPHENYL-4-YL)-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
125	OH SHOP	5-(4-HYDROXYMETHYL-PHENYL)-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	
126	ا ا	5-FURAN-3-YL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
127		5-BENZOFURAN-2-YL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	
	~	5-PYRIDIN-2-YL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++

<u> </u>	MOI STRUCTURE		PCT/CA02/00
	MOLSTRUCTURE	COMPOUND NAME	IC50
129	O=S, NH O, NH O, NH O	5-(4-NITRO-PHENYL)-3-(PYRIDINE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++
130	N-CH ₃	3-[(BENZOFURAN-2-CARBONYL)- METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+
131	CH ₃ OH OH	3-[(2,4-DIMETHYL-BENZOYL)-METHYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
132	CI CI O S O O O O O O O O O O O O O O O O O	3-[[5-(2-CYANO-PHENYL)-THIOPHEN-2- YLMETHYL]-(2,4-DICHLORO-BENZOYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
133	F S OH	5-(4-FLUORO-PHENYL)-3-(PYRIDINE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
134	H,C H,S OH	5-[2-(4-CHLORO-PHENYL)-VINYL]-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	

	MOLSTRUCTURE	COMPOUND NAME	IC50
135	HON SOH	3-BENZENESULFONYLAMINO-5-(4- FLUORO-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	+++
136	CH ₃ CH ₃ CH ₃ CH ₃	3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
137	OES. NH OH	5-PHENYL-3-(2-VINYL- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	++
138	F Br O S NH OH OH	3-(4-BROMO-2,5-DIFLUORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
139		3-(2-ACETYLAMINO-4-METHYL- THIAZOLE-5-SULFONYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
140	O CH ₃ O ≥ S O NH OH	3-(4-ACETYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
141	OF FFOH	3-(4-FLUORO-2-TRIFLUOROMETHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	· •
142	CH, O=S, OH OH OH	3-(2-METHOXY-4-METHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
143	1	3-(3,4-DIFLUORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	-++

144 145 146 147 148 149 140 140 140 140 140 140 140		MOLSTRUCTURE	COMPOUND NAME	IC50
3-(4-FLUORO-3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-(2-AMINO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 146 3-(3-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 147	144	PH,C O≅S,NH Qa	MLSULFAMOYL)-5-(4-CHLORO-PHENYL)- 12-METHYL-FURAN-3-CARBOXYLIC ACID	++
3-(2-AMINO-BENZENESULFONYLAMINO)- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-(3-NITRO-BENZENESULFONYLAMINO)- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 147 0=N 0=N 0=N 0=N 0=N 0=N 0=N 0=N 0=N 0=	145	1 1""	3-(4-FLUORO-3-TRIFLUOROMETHYL- BENZENESULFONYLAMINO)-5-PHENYL-	
3-(3-NITRO-BENZENESULFONYLAMINO)- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID +++	146	1 /	5-PHENYL-THIOPHENE-2-CARBOXYLIC	+++
O=N O O=S	147			
3-(4-NITRO-BENZENESULFONYLAMINO)- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID		O=S, NH		

	MOLSTRUCTURE	T	PC 1/CA02/00
-	INICLOTRUCTURE	COMPOUND NAME	IC50
			·
149	CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
150	CH _s O=s.O NH OH	5-(3-CYANO-BENZYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+
151	F S NH OH	5-PHENYL-3-(2,4,6-TRIFLUORO- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
	CH _s ON OH OH OH OH	3-(4-METHOXY-2-NITRO- BENZENESULFONYLAMINO)-5-PHENYL-	
152			++

	MOI STRUCTURE		PCT/CA02/00
	MOLSTRUCTURE	COMPOUND NAME	IC50
153	CI C	5-PHENYL-3-(2,3,4-TRICHLORO- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
154	H ₃ C O CH ₃	5-(2-CARBOXY-5-PHENYL-THIOPHEN-3- YLSULFAMOYL)-2-METHYL-FURAN-3- CARBOXYLIC ACID METHYL ESTER	***
155	CH, CH,	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2-METHYL-1,5-DIPHENYL-11-PYRROLE-3-CARBOXYLIC	+++
158	O NH OH	5-PHENYL-3-{[4-(3-TRIFLUOROMETHYL- PHENYL)-PIPERAZINE-1-CARBONYL]- AMIN}-THIOPHENE-2-CARBOXYLIC ACID	++

	0 02/100851		PCT/CA02/00
	MOLSTRUCTURE	COMPOUND NAME	IC50
157	ONH OH	3-{[4-(4-FLUORO-PHENYL)-PIPERAZINE- 1-CARBONYL]-AMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+
158	H ₃ C CH ₃ ON CH ₃ OH	3-{[4-(2,6-DIMETHYL-PHENYL)- PIPERAZINE-1-CARBONYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
159	CI ZY OH OH	3-{[4-(2-CHLORO-PHENYL)-PIPERAZINE- 1-CARBONYL]-AMINO}-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
160	1	3-{[4-(3-CHLORO-PHENYL)-PIPERAZINE- 1-CARBONYL]-AMINO}-5-PHENYL-	++

		MOLSTRUCTURE	COMPOUND NAME	IC50
16	1	HO S S OH	4,4'-BIS-(TOLUENE-2-SULFONYLAMINO)- [2,2']BITHIOPHENYL-5,5'-DICARBOXYLIC ACID	+++
162	2	H ₂ C CH ₃	3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
163	- 1	H,C, O, CH, O, C	5-(1-DIMETHYLSULFAMOYL-1#H!- PYRAZOL-4-YL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++
164			5-(3-AMINO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++
165		•	5-(4-AMINO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++
166		ĊH ₃	5-(4-ACETYL-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	-++

	MOLSTRUCTURE	COMPOUND NAME	IC50
		The state of the s	1000
	çн ,		
) CH ₃		
	0 NH		
	O NH O=S NH CH		
	OH	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-	
	s	MLSULFAMOYL)-2,5-DIMETHYL-1H-	
167		PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER	++
ļ	.H,C~0~0		
	HC N		
	O=S, ONH OH Q	1	
	OH G	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-	
		MLSULFAMOYL)-5-(4-CHLORO-PHENYL)-	
168		3-METHYL-1-PHENYL-1H-PYRROLE-2- CARBOXYLIC ACID ETHYL ESTER	++
	, OH		
	NH		
	OH	(0	
		3-(3,5-DICHLORO-4-HYDROXY- BENZENESULFONYLAMINO)-5-PHENYL-	
169	•		++
	તમુદ્		
	H'i		
	SOH		
	N. N	5-(1#H!-PYRAZOL-4-YL)-3-(TOLUENE-2-	
170	"	SULFONYLAMINO)-THIOPHENE-2-	+++
	H & >		
	N-S		ł
	S OH	·	
	OH OH	5-(3-HYDROXY-PHENYL)-3-(TOLUENE-2-	.
171		SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
	OU O		
	CH3O CH3	·	,
		2 METHA (2 METHA) DI MANA	
	0	3-[METHYL-(3-METHYL-BUTYRYL)- AMINO]-5-PHENYL-THIOPHENE-2-	
172	~	0.45560.00.00.00	+++

	MOLSTRUCTURE	· COMPOUND NAME	IC50
	_		
173	CH,O F N OH	3-{[2-(4-FLUORO-PHENYL)-ACETYL]- METHYL-AMINO}-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+++
174	CH ₃ O=S, OH OH OH	3-(4-PENTYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
175	CH ₃ O N OH	3-(METHYL-PHENYLACETYL-AMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC	+++
176	OF SHOP	3-{2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)- BENZENESULFONYLAMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	•+
177		3-(4-METHYL-2-NITRO- BENZENESULFONYLAMINO)-5-PHENYL-	+

	MOLSTRUCTURE	COMPOUND NAME	IC50
178	N-S, OH	5-THIAZOL-2-YL-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
179	HN OH OH	5-PHENYL-3-[3-(3-PHENYL-PROPYL)- UREIDO]-THIOPHENE-2-CARBOXYLIC ACID	++
180	O NH OH S OH	3-[(3,4-DIHYDRO-1H-ISOQUINOLINE-2- CARBONYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
181		3-{[4-(4-METHOXY-PHENYL)-PIPERAZINE- 1-CARBONYL]-AMINO}-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+-4
182	CIH NOH	3-{[4-(6-METHYL-PYRIDIN-2-YL)- PIPERAZINE-1-CARBONYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC	

	MOLSTRUCTURE	COMPOUND NAME	IC50
492	OTH NO OH OH	3-{[4-(4-CHLORO-BENZYL)-PIPERAZINE- 1-CARBONYL]-AMINO}-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
183		HYDROCHLORIDE	++
184	H ₃ C OH	5-(5-METHYL-PYRIDIN-2-YL)-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
185	H ₃ C CH ₃	3-[ETHYL-(4-METHYL-BENZOYL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
186	~	3-[(3-CHLORO-THIOPHENE-2- CARBONYL)-METHYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
187	<u> </u>	3-[(2-BROMO-BENZOYL)-METHYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	* *

	MOLSTRUCTURE	COMPOUND NAME	IC50
188	H ₃ C, NOOH	3-[(4-BUTYL-BENZOYL)-METHYL-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
189	H-ij-OH CI	3-(2-CHLOROMETHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
190	H ₃ C H ₂ S OH	5-(4-HYDROXY-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
191	H ₃ C N-S OH OH	5-(5-CHLORO-PYRIDIN-2-YL)-3- (TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
192	CH ₃ CH ₃ CH ₃	5-(4-CHLORO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE-	++
193	N.	5-(4-CYANO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	

	MOLSTRUCTURE	COMPOUND NAME	IC50
194	CH ₃ CH ₃	3-[METHYL-(4-METHYL-BENZOYL)- AMINO]-5-(4-NITRO-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	++
134	0	THIOFHENE-2-CARBOXYLIC ACID	77
195		5-(4-HYDROXYMETHYL-PHENYL)-3- [METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	++
196	0 0	3-[METHYL-(4-METHYL-BENZOYL)- AMINO]-5-(3-NITRO-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	+++
197	-	5-(4-FLUORO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	+++
198	O113	5-(4-METHOXY-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	++
199	1,20	3-[METHYL-(4-METHYL-BENZOYL)- AMINO]-5-#PI-TOLYL-THIOPHENE-2- CARBOXYLIC ACID	++
200	121	5-(4-AMINO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
201	CI OH SOOH	3-[CYCLOPENTYL-(2,4-DICHLORO- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
202	H _s C H _s C OH OH	5-BENZO[1,3]DIOXOL-5-YL-3-(TOLUENE- 2-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
203	HO CH ₃	3-[(2-HYDROXY-ETHYL)-(4-METHYL- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
204	H ₃ C CI CI CI OH	3-[(2,4-DICHLORO-BENZOYL)-ISOBUTYL- AMINO]-5-PHENYL-THIOPHENE-2-	+++
205		3-[(2-METHOXY-4-METHYL-BENZOYL)- METHYL-AMINO]-5-PHENYL-THIOPHENE-	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
206	H ₃ C OH CH ₃	5-(3-CYANO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	+++
207	H ₃ C. OH CH ₃	5-(2-CHLORO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	++
208	CI N-OO S OH	3-[(2,4-DICHLORO-BENZOYL)-PHENYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
209		3-[4-(TRIFLUOROMETHYL- BENZOYL)METHYLAMINE]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
210	H ₃ C CH ₃ CI	3-[(4-CHLORO-BENZOYL)-ISOPROPYL- AMINO]-5-PHENYL-THIOPHENE-2-	+++
211	~	3-[ISOPROPYL-(4-METHYL-BENZOYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	, +++

	MOLSTRUCTURE	COMPOUND NAME	IC50
212	H ₃ C. OH CH ₃	5-(3,5-DIFLUORO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	·
213	H ₃ C. OH CH ₃	5-(3-FLUORO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	+++
214	H ₃ C OH CH ₃	5-(2,4-DIFLUORO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	++
215	HO •	5-(4-HYDROXY-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	+++
216	F CO CO	3-[METHYL-(4-METHYL-BENZOYL)- AMINO]-5-(4-TRIFLUOROMETHOXY- PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	++
217	OH	5-(2-HYDROXY-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++
218	0	3-[(2-CHLORO-BENZOYL)-ISOPROPYL- AMINO}-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
219	H,C CH, CH, CH, CH, CH, CH, CH, CH, CH,	3-[(3,5-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
220	Br CH₃ O NH OH S	3-(4-BROMO-2-METHYL- BENZENESULFONYLAMINO)-5-PHENYL-	
221	CI C	3-(5-CARBOXY-4-CHLORO-2-FLUORO- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+
222		5-PHENYL-3-(2,3,4-TRIFLUORO- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	++
223		3-(4-BROMO-2-FLUORO- BENZENESULFONYLAMINO)-5-(4- ISOBUTYL-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	

	MOLSTRUCTURE	COMPOUND NAME	IC50
224	H,C OH OH	3-(4-BROMO-2-METHYL- BENZENESULFONYLAMINO)-5-(4- ISOBUTYL-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	
225	H ₃ C-O O O O O O O O O O O O O O O O O O O	5-(4-ISOBUTYL-PHENYL)-3-(3-METHOXY- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+
226	H ₃ C CH ₃ F OH	3-[(4-FLUORO-BENZOYL)-ISOPROPYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
227	FF O S S O NH OH	3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)- BENZENESULFONYLAMINO]-5-(4- ISOBUTYL-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	+
228	H ₃ C S N	3-(2-CHLORO-4-CYANO- BENZENESULFONYLAMINO)-5-(4- ISOBUTYL-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	+

	MOLSTRUCTURE	COMPOUND NAME	IC50
229	H ₃ C S S OH CH ₃	5'-ACETYL-4-(TOLUENE-2- SULFONYLAMINO)-[2,2']BITHIOPHENYL-5- CARBOXYLIC ACID	+++
230	N-S OH,	5-BENZO[B]THIOPHEN-2-YL-3-(TOLUENE- 2-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
231	CH ₃	5-(4-BUTYL-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
232	H _s C OH CH _s	5-(4-ETHYL-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
233	~	3-[BENZYL-(2,4-DICHLORO-BENZOYL)- AMINO]-5-PHENYL-THIOPHENE-2-	· +++
234	H ₃ C CH ₃ CH ₃ CH ₃ CH ₃	3-[(4-CHLORO-2-METHYL-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL-	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
235	H ₃ C CH ₃ O CH ₃ O OH	3-[(2,4-DIMETHYL-BENZENESULFONYL)- METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	
236	H ₃ C S OH CH ₃	5-(4-ACETYL-PHENYL)-3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
237	н,с	5-(4-ACETYL-PHENYL)-3-(TOLUENE-4- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
238	0	5-(4-ACETYL-PHENYL)-3-(4-CHLORO- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
239	GH ₃ C [^] CH ₃	5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID #TERTI-BUTYL ESTER	++
240	~	3-[(2,4-DIMETHYL-BENZENESULFONYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+ +
241		3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+ +

	MOLSTRUCTURE	COMPOUND NAME	IC50
242	CH _s O=S=O NH OH	3-ETHANESULFONYLAMINO-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
243	H ₃ C CH ₃ F S OH	3-[ISOPROPYL-(4-TRIFLUOROMETHYL- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
244	H ₃ C-CH ₃ CI	3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL- BUT-2-ENYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
245		3-[(2,6-DICHLORO-PYRIDINE-3- CARBONYL)-METHYL-AMINO]-5-PHENYL-	++
246	0	3-[(6-CHLORO-PYRIDINE-3-CARBONYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+
1 1	× I	3-[(4-TERT-BUTYL-BENZOYL)-METHYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	

	MOLSTRUCTURE	COMPOUND NAME	IC50
248	HO S OH	5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
249	CH ₃ OH CH ₃	5-(4-ETHOXY-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
250	H ₃ C CH CH	3-[(2,6-DICHLORO-PYRIDINE-3- CARBONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
251	~	3-[(BENZO[B]THIOPHENE-2-CARBONYL)- METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	++
252	~	3-[METHYL-(NAPHTHALENE-2- CARBONYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
253		3-[(3,4-DICHLORO-BENZOYL)-METHYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
254	CI N-CH, OH	3-[(3,5-DICHLORO-BENZOYL)-METHYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
255	H ₃ C Br—V-CH ₃ OH	3-[(4-BROMO-3-METHYL-BENZOYL)- METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+++
256	N-CH ₃	3-[(3-CHLORO-BENZO[B]THIOPHENE-2- CARBONYL)-METHYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
257	O=NO-CH ₃ OH	3-[METHYL-(4-METHYL-3-NITRO- BENZOYL)-AMINO]-5-PHENYL-	++
258	H ₂ N OH CH ₃	5-(4-CARBAMOYL-PHENYL)-3-(2,4- DIMETHYL-BENZENESULFONYLAMINO)-	++
259	H,N SOOH	5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE- 4-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
260	HN S OCH3	5-(1H-INDOL-5-YL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++
261	H ₃ C CH ₃ CI	3-[#SEC!-BUTYL-(2,4-DICHLORO- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
262	H ₃ C CH ₃ CH ₃ OH CH ₃	3-[(2,4-DIMETHYL-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
263	N-N-1N3 S OOH CH3	5-(4-AZIDO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	+++
264	CH ₃ CI N-OCI OH	3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL- ETHYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	
265	0	5-(4-CARBAMOYL-PHENYL)-3-(4- CHLORO-BENZENESULFONYLAMINO)-	+++

	MOLSTRUCTURE	COMPOUND NAME	C1/CA02/00
-	MOLSTROCTORE	COMPOUND NAME	IC50
266	H,C, O OH CH,	5-(2-FLUORO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	+++
267	H ₃ C O CH ₃	3-[METHYL-(4-METHYL-BENZOYL)- AMINO]-5-#O!-TOLYL-THIOPHENE-2- CARBOXYLIC ACID	+++
268	H ₃ C OH CH ₃	3-[METHYL-(4-METHYL-BENZOYL)- AMINO]-5-M-TOLYL-THIOPHENE-2- CARBOXYLIC ACID	.
269	H,C OH CH,	5-(3-CHLORO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE-	
270	H ₃ C OH CH ₃	5-(3,4-DIFLUORO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE-	+++
271	1'2'`	5-(3-AMINO-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE-	++

MOLSTRUCTURE	COMPOUND NAME	IC50
H ₃ C OH CH ₃	5-(3-ACETYL-PHENYL)-3-[METHYL-(4-	
	2-CARBOXYLIC ACID	++
H _s C OH CH _s	5-(3-HYDROXY-PHENYL)-3-[METHYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	+++
H ₃ C O OH CH ₃	3-[METHYL-(4-METHYL-BENZOYL)- AMINO]-5-(3-TRIFLUOROMETHYL- PHENYL)-THIOPHENE-2-CARBOXYLIC	
	ACID	+++
H ₃ C OH CH ₃	3-[METHYL-(4-METHYL-BENZOYL)- AMINO]-5-(4-TRIFLUOROMETHYL- PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
	AMINO]-5-PHENYL-THIOPHENE-2-	+
F-CHS OH	3-[METHYL-(2,4,6-TRIFLUORO-BENZOYL)-	
	CARBOXYLIC ACID	++
	H ₃ C CH ₃ OCH	F GON CH, 5-(3-ACETYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO)-THIOPHENE-2-CARBOXYLIC ACID 5-(3-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO)-THIOPHENE-2-CARBOXYLIC ACID 3-[METHYL-(4-METHYL-BENZOYL)-AMINO)-THIOPHENE-2-CARBOXYLIC ACID 1-1-CH ₃ 3-[METHYL-(4-METHYL-BENZOYL)-AMINO)-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID 3-[METHYL-(4-METHYL-BENZOYL)-AMINO)-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID 3-[METHYL-(4-METHYL-BENZOYL)-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-[METHYL-(2-4-FIRIFLUOROMETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID 3-[METHYL-(2-4-6-TRIFLUORO-BENZOYL)-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

	MOLSTRUCTURE	COMPOUND NAME	IC50
278	N-CH ₃	3-[(2,3-DIFLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
279	N-CH ₃	3-[(3-FLUORO-4-TRIFLUOROMETHYL- BENZOYL)-METHYL-AMINO]-5-PHENYL-	++
280	F CH ₃ OH OH	3-[(2,3-DIFLUORO-4-METHYL-BENZOYL)- METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+++
281	F F F F OH OH	3-[(2-FLUORO-4-TRIFLUOROMETHYL- BENZOYL)-METHYL-AMINO]-5-PHENYL-	
282	0	5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE- 2-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
283	H ₃ C N CH ₃	5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4- METHYL-BENZOYL)-AMINO]-THIOPHENE- 2-CARBOXYLIC ACID	+++
284	H ₃ C Br	3-[(2-BROMO-4-CHLORO-BENZOYL)- METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+++
285	H,C OH OH CH ₃	3-(2,6-DIMETHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
286	H ₃ C CH ₃ .	3-[METHYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
287	O-CH ₃	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
288	N S O CH3	5-(4-CYANO-PHENYL)-3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)-	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
289	N S OH	3-(4-CHLORO- BENZENESULFONYLAMINO)-5-(4- CYANO-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	+++
290	N CH ₃	5-(4-CYANO-PHENYL)-3-(TOLUENE-4- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID	
291	H ₃ CCOCH ₃	5'-ACETYL-4-(2,4-DIMETHYL- BENZENESULFONYLAMINO)- [2,2]BITHIOPHENYL-5-CARBOXYLIC ACID	+++
292		5'-ACETYL-4-(2,6-DIMETHYL- BENZENESULFONYLAMINO)- [2,2]BITHIOPHENYL-5-CARBOXYLIC ACID	***
293	H ₃ C S CH ₃	3-[METHYL-(4-METHYL-THIOPHENE-2- CARBONYL)-AMINO]-5-PHENYL-	++
294	Čı ,	5-(3-CHLORO-PHENYL)-3-[(2,4- DICHLORO-BENZOYL)-ISOPROPYL- AMINO]-THIOPHENE-2-CARBOXYLIC ACID	-+-

	MOLSTRUCTURE	COMPOUND NAME	IC50
301	H ₃ C CH OH	3-[(2-HYDROXY-4-METHYL-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
302	H ₃ C. OH CH ₃	3-[METHYL-(4-METHYL-BENZOYL)- AMINO]-5-PYRIDIN-3-YL-THIOPHENE-2- CARBOXYLIC ACID	++
303	н,с в он сн,	5'-ACETYL-4-[METHYL-(4-METHYL- BENZOYL)-AMINO]-[2,2']BITHIOPHENYL-5- CARBOXYLIC ACID	+++
304	F->F	3-[ISOPROPYL-(4-METHYL-BENZOYL)- AMINO]-5-(3-TRIFLUOROMETHYL- PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	+++
305	J. 5	3-[ISOPROPYL-(4-METHYL-BENZOYL)- AMINO]-5-M-TOLYL-THIOPHENE-2- CARBOXYLIC ACID	+++
306	OH .	3-[(2-BROMO-4-CHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
			1.555
307	H ₃ C CH	3-[(4-CHLORO-2-FLUORO-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
308	H ₃ C CH ₃ OCH ₃ OCH ₃	3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)-4-METHYL- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
309	H ₃ C CH ₃ CH ₃ Br OH	3-[(2-BROMO-4-METHYL-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
310	H ₃ C CH ₃ CI	3-[(4-CHLORO-2-IODO-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
311	H _s C CH Sen	3-[(4-CYANO-BENZOYL)-ISOPROPYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
312	H ₂ C CH ₃	3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]- 5-[4-(2-CARBOXY-VINYL)-PHENYL]- THIOPHENE-2-CARBOXYLIC ACID.	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
313	H ₃ C-CH OH OH	3-[(4-CHLORO-2-HYDROXY-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
314	H ₃ C N CI	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-4-METHYL-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
315	H ₃ C CH ₃ OH	5-#TERT!-BUTYL-3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	++
316	S T	3-[ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+
317	S To	3-[ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
318	· ·	5-[4-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4- METHYL-BENZOYL)-PROPYL-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	**

WO 02/100851 PCT/CA02/00876

	MOLSTRUCTURE	COMPOUND NAME	IC50
319	HN-SO-CH,	5-BENZOFURAN-2-YL-3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
320	но н,с о он в о он но	3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)-5-(4- HYDROXYMETHYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	+++
321	о нс-s	3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)-5-(4- METHANESULFONYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	+++
322	H,C CH,	5-[4-(2-CARBOXY-VINYL)-PHENYL]-3-(2,4- DIMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID	+++
323	~ "	3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]- 5-[3-(2-CARBOXY-VINYL)-PHENYL]- THIOPHENE-2-CARBOXYLIC ACID	++
324	0	3-[ISOPROPYL-(2,4,6-TRIMETHYL- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
325) v	5-[3-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4- METHYL-BENZOYL)-PROPYL-AMINO]- THIOPHENE-2-CARBOXYLIC ACID.	· •

	MOLSTRUCTURE	COMPOUND NAME	IC50
326	H ₃ C CH ₃ F N OH F	3-[(2-FLUORO-4-TRIFLUOROMETHYL- BENZOYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
327	~ .	3-[#TERT!-BUTYL-(2,4-DICHLORO- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
328	0	3-[(2-AMINO-4-CHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
329	0	3-[(4-CHLORO-2-NITRO-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
330		3-[(4-METHYL-BENZOYL)-(3- TRIFLUOROMETHYL-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
331	0 .	3-[(3-FLUORO-4-METHYL-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
332	H,C H,S O OH HO	5-(4-CARBOXY-PHENYL)-3-(2,4-DIMETHY L-BENZENESULFONYLAMINO)- THIOPHENE-2 -CARBOXYLIC ACID	+++
333	CI N-OOH	3-[CYCLOPROPYL-(2,4-DICHLORO- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
334	~	3-[(3-TERT-BUTYL-BENZYL)-(4-METHYL- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
335	~	3-[(3-CHLORO-BENZYL)-(4-METHYL- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++ +
336		3-[(2,4-DIFLUORO-BENZYL)-(4-METHYL- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	, +++

	MOLSTRUCTURE	COMPOUND NAME	IC50
337	H ₃ C CH ₃ CH F OH	3-[(4-CHLORO-2,5-DIFLUORO-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
338	CI CH ₃ CH ₃ CH ₃ CH ₃	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-(2-METHYL- ALLYL)-THIOPHEN E-2-CARBOXYLIC ACID	+++
339	V OH	3-{ALLYL-[2-(4-CHLORO-PHENYL)- ACETYL]-AMINO}-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	·
340		3-[BENZYL-(4-METHYL-BENZOYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
341	~	3-[(4-CHLORO-BENZYL)-(4-METHYL- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	

	MOLSTRUCTURE	COMPOUND NAME	IC50
342	OH CH ₃	3-[(4-METHYL-BENZOYL)-(4-NITRO- BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+++
343	H ₃ C OH CH ₃	3-[(4-METHYL-BENZOYL)-(2-METHYL- BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+++
344	O- OCH ₃	3-[(3-METHOXY-BENZYL)-(4-METHYL- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
345		3-[(2-CHLORO-BENZYL)-(4-METHYL- BENZOYL)-AMINO]-5-PHENYL-	+++
346	н,с сн,	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-ISOBUTYL- THIOPHENE-2-CARB OXYLIC ACID	

	MOLSTRUCTURE	COMPOUND NAME	IC50
		·	
	O=N=CH ₂	<u>.</u>	
347	0	3-[ALLYL-(2-NAPHTHALEN-2-YL-ACETYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+
	CI		
348	O N CH ₂	3-{ALLYL-[2-(2,4-DICHLORO-PHENYL)- ACETYL]-AMINO}-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	++
	F		
	CI O= CH ₂ OH	3-{ALLYL-[2-(2-CHLORO-4-FLUORO-	
349	v	PHENYL)-ACETYL]-AMINO}-5-PHENYL-	++
	CI CI CI CH ₂		
350	.]	3-{ALLYL-[2-(3,4-DICHLORO-PHENYL)- ACETYL]-AMINO}-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	++
	F		
351	ا ا	3-{ALLYL-[2-(2,4-DIFLUORO-PHENYL)- ACETYL]-AMINO}-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
	_ 		
352	F F CH ₂	3-{ALLYL-[2-(4-TRIFLUOROMETHYL- PHENYL)-ACETYL]-AMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
353	CI O= CH ₂ OH	3-{ALLYL-[2-(2,6-DICHLORO-PHENYL)- ACETYL]-AMINO}-5-PHENYL-THIOPHENE-	++
354	CH ₃ O=CH ₂ OH	3-[ALLYL-(2-M-TOLYL-ACETYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
355	H ₃ C-CH ₆ CI NOH OCH ₃ OH	5-(4-ACETYL-PHENYL)-3-[(2,4-DICHLORO- BENZOYL)-ISOPROPYL-AMINO]-	

	MOLSTRUCTURE	COMPOUND NAME	IC50
356	H ₃ C-CH ₀ CI OH	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-(4-FLUORO- PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	1-1-1
357	H _s C CH _s Cl	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-M-TOLYL- THIOPHENE-2-CARBOXYLIC ACID	++ +
358	H ₃ C CH ₀ CI S OH	5'-ACETYL-4-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-[2,2']BITHIOPHENYL-	+++
359	F	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-(3- TRIFLUOROMETHYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	+++
360	J. 13	4-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5'-METHYL- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID	+++
361	н,с.	3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)-5-(4- METHOXY-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
362	H ₃ C=CH ₃ N=O S OH	3-(CYCLOHEXANECARBONYL- ISOPROPYL-AMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
363	C C C C C C C C C C C C C C C C C C C	3-{(2,4-DICHLORO-BENZOYL)-[1-(2,4- DICHLORO-BENZOYL)-PIPERIDIN-4-YL]- AMINO}-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
364	CH ₃ CH ₃ CH ₃ CH ₃ CH ₃ CH ₃	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(4-METHYL-BENZOYL)-AMINO]- PIPERIDINE-1-CARBOXYLIC ACID #TERT!-BUTYL ESTER	+++
365	CH ₃ , CI	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(2,4-DICHLORO-BENZOYL)-AMINO]- PIPERIDINE-1-CARBOXYLIC ACID #TERTI-BUTYL ESTER	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
	α-		
	_ ·		
	N CH ₃		
366	STOH	3-[(4-METHYL-BENZOYL)-PIPERIDIN-4-YL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
500	H-s CH,	CARBOXTEIC ACID	
	s of one		
367		5'-ACETYL-4-(2,4-DIMETHYL- BENZENESULFONYLAMINO)- [2,3']BITHIOPHENYL-5-CARBOXYLIC ACID	
	СІН	· .	
	√N ~a		
368	0	3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN- 4-YL-AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
	N-s		
	0=\$=0 CH	5-(4-METHANESULFONYLAMINO- PHENYL)-3 -(TOLUENE-2-SULFONYLAMINO)- THIOPHEN	
369		E-2-CARBOXYLIC ACID	++
	D-S CH,		
370	0 .	3-(4-FLUORO-2-METHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
		3-[(3-METHYL- CYCLOHEXANECARBONYL)-ISOPROPYL-	
371	s	AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+

	MOLSTRUCTURE	COMPOUND NAME	IC50
372	H-si CH,	3-(4-CHLORO-2-METHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
373	CI CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH	3-{(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-(4- METHANESULFONYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	+++
374	CI CH ₃ CH ₃ CH ₃ CH ₃ CH ₄ CH ₃ CH ₄ CH ₅ CH	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-(4- METHANESULFINYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	+++
375	CI CI CH _s N CH _s N HO	5-(4-CARBOXY-PHENYL)-3-[(2,4- DICHLORO-BENZOYL)-ISOPROPYL- AMINOJ-THIOPHENE-2-CARBOXYLIC ACID	· +++
376		5-BENZOFURAN-2-YL-3-[(2,4-DICHLORO- BENZOYL)-ISOPROPYL-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
377	H ₃ C CH ₃ CH ₃	3-[(2-ACETOXY-4-METHYL-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
378	H ₃ C-CH ₃ NHCOOH	3-[ISOPROPYL-(2-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
379	H ₃ C CH ₃ O CH ₃ O CH ₃	3-[ISOPROPYL-(2-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
380	~	3-(CYCLOHEPTANECARBONYL- ISOPROPYL-AMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
381	F-V _F	3-[ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5-(3- TRIFLUOROMETHYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	
382	CH, CH, 6H	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-METHYL-	

wo	02/100851	P	CT/CA02/00876
	MOLSTRUCTURE	COMPOUND NAME	IC50
383	H ₃ C CH ₃ CH ₃ NO OH	3-[ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5-(3- NITRO-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	
. 384	O N-CH ₃ OH	3-[(3-CYCLOPENTYL-PROPIONYL)- METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+++
385	CH ₃ OH OH	3-(BUTYRYL-METHYL-AMINO)-5-PHENYL-	++
386	`	3-(METHYL-PENT-4-ENOYL-AMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
387	0	3-[ISOPROPYL-(5-METHYL-3-OXO-3H- ISOINDOL-1-YL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
	H ₃ C CH ₃ ON-CH ₃ OH	3-[METHYL-(3-METHYL-BUTYRYL)- AMINO]-5-PHENYL-THIOPHENE-2-	
388		CARBOXYLIC ACID	+++
389	H ₃ C OH N-CH ₃ OH	3-(METHYL-PENTANOYL-AMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
309		ACID	+++
390	CH ₃ CH ₃ OH	3-[METHYL-(4-METHYL-PENTANOYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
391	O=\CH ₃	3-(CYCLOPENTANECARBONYL-ETHYL- AMINO)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	* +
392	~ .	3-[(3-CYCLOPENTYL-PROPIONYL)- ETHYL-AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
	O= CH ₃		,,,,,,
393	S I	3-(CYCLOBUTANECARBONYL-ETHYL- AMINO)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
394	CH _s CH _s OH OH	3-(BUT-2-ENOYL-ETHYL-AMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
395	H ₃ C CH ₃ CH ₃ CH ₃ CH ₃	3-[ISOPROPYL-(4-METHYL-2-VINYL- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
396	H ₃ C CH ₃ OH	3-[ISOPROPYL-(4-METHYL-CYCLOHEX-1- ENECARBONYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
	CH ₃ O=CH ₂ OH		
397	<u> </u>	3-(ALLYL-HEXANOYL-AMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
398	O=N=CH ₂	3-(ALLYL-CYCLOBUTANECARBONYL- AMINO)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+
399	H ₃ C O= N=CH ₂ OH	3-(ALLYL-PENTANOYL-AMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
400	•	3-[ALLYL-(4-METHYL-PENTANOYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
401	~	3-[ALLYL-(2-CYCLOPENTYL-ACETYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
402	STOR	3-[(2-HYDROXY-4-METHYL- CYCLOHEXANECARBONYL)-ISOPROPYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
403	CH _S CI	3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL- ETHYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+++
404	CH _S CI N-OCI OCHSCI	3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL- ETHYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+++
405	H ₃ C CH ₃ CH ₃ OH	3-[ISOPROPYL-(3-METHYL-CYCLOPENT- 3-ENECARBONYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
406	F ·	3-[(2-BENZYLOXY-4-METHYL-BENZOYL)- ISOPROPYL-AMINO]-5-(3- TRIFLUOROMETHYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	+++
407	S TOH	3-[(2,4-DIMETHYL- CYCLOHEXANECARBONYL)-ISOPROPYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
			1
	H ₃ C CH ₃ CH ₃		
408	S TOH	3-[ISOPROPYL-(3-METHYL- CYCLOPENTANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
	H ₃ C (CH ₃ CH ₃		5
409	N HO	 3-[(2-HYDROXY-4-METHYL- CYCLOHEXANECARBONYL)-ISOPROPYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
	F. F.		
	F		
	CH ₃		
110	~	5-PHENYL-3-[PROPIONYL-(4- TRIFLUOROMETHYL-BENZYL)-AMINO]-	
410		THIOPHENE-2-CARBOXYLIC ÁCID	++ .
411		3-[ISOBUTYRYL-(4-TRIFLUOROMETHYL- BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	.
	FFF O CH ₃ CH ₃		
412		3-[(3-METHYL-BUTYRYL)-(4- TRIFLUOROMETHYL-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
413	FFF NOH	3-[CYCLOPROPANECARBONYL-(4- TRIFLUOROMETHYL-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
414	FF F OH	3-[CYCLOBUTANECARBONYL-(4- TRIFLUOROMETHYL-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
415	FFF N CH _s	3-[BUTYRYL-(4-TRIFLUOROMETHYL- BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	· ++
416	0.	3-[(2-CYCLOPENTYL-ACETYL)-(4- TRIFLUOROMETHYL-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
417	н,с снан, С сн,	3-[(4-TERT-BUTYL-BENZYL)-PROPIONYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
418	CH,	3-[(4-NITRO-BENZYL)-PROPIONYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
419	O CH ₃ CH ₃ O CH ₃	3-[(3-METHYL-BUTYRYL)-(4-NITRO- BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+++
420		3-[CYCLOPROPANECARBONYL-(4- NITRO-BENZYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
421	CH _s CH _s CH _s CH _s	3-[(2-CHLORO-BENZYL)-ISOBUTYRYL- AMINO]-5-PHENYL-THIOPHENE-2-	

	MOLSTRUCTURE	COMPOUND NAME	IC50
422	CI CH ₃ CH ₃ CH ₃	3-[(2-CHLORO-BENZYL)-(3-METHYL- BUTYRYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
423	CI NOH	3-[(2-CHLORO-BENZYL)- CYCLOPROPANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	-
424	H ₃ C CH ₃ H N H N H	3-[(ADAMANTANE-1-CARBONYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+
425	CI CI OH	3-[(2-CHLORO-BENZYL)- CYCLOBUTANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
426	H ₃ C CH ₃	3-[ACETYL-(2-METHYL-BENZYL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
427	н,с С С С С С С С С С С С С С С С С С С С	3-{(2-METHYL-BENZYL)-PROPIONYL- AMINO}-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
	MOESTROOTURE	COMPOUND NAME	1030
	_	·	
428	H ₃ C CH ₃ OH OH	3-[(2-HYDROXY-4-METHYL-BENZOYL)- ISOPROPYL-AMINO]-5-(3- TRIFLUOROMETHYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	
429	H ₃ C-ON-OH	3-[(1-ACETYL-PIPERIDIN-4-YL)-(2,4- DICHLORO-BENZOYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
430	N-N	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-[4-(1#H!- TETRAZOL-5-YL)-PHENYL]-THIOPHENE- 2-CARBOXYLIC ACID	· +++
431	0	3-[(2-CYANO-4-METHYL-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
432	H _s C — OH	3-[CYCLOBUTANECARBONYL-(2- METHYL-BENZYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
433	н _з с Сн,	3-[BUTYRYL-(2-METHYL-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
434	CH ₃ OCH ₃ OH	3-[ACETYL-(3-METHYL-BENZYL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
435	CH, OH	3-[CYCLOBUTANECARBONYL-(4- METHYL-BENZYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
436	FFF NOH	3-[CYCLOHEXANECARBONYL-(4- TRIFLUOROMETHYL-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
437	H ₃ C CH ₆ H ₃ CH ₃ CH ₃ OH	3-[(4-TERT-BUTYL-BENZYL)- ISOBUTYRYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
438	H, HC CH,	3-[(4-TERT-BUTYL-BENZYL)- CYCLOPROPANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
439	H ₃ CC CH ₃	3-[(4-TERT-BUTYL-BENZYL)- CYCLOBUTANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
440	H ₃ CC CH ₃ CH ₃ OH	3-[(4-TERT-BUTYL-BENZYL)-BUTYRYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
441	H _s tes ch _s	3-[(4-TERT-BUTYL-BENZYL)- CYCLOHEXANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
442		3-[(4-TERT-BUTYL-BENZYL)-(2- CYCLOPENTYL-ACETYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
443	V	3-[(2-CYCLOPENTYL-ACETYL)-(4-NITRO- BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	
444		3-[(2-CHLORO-BENZYL)- CYCLOHEXANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
445	~	3-[(2-CYCLOPENTYL-ACETYL)-(3- METHYL-BENZYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	/ F++

	MOLSTRUCTURE .	COMPOUND NAME	IC50
446	СН ₃ — СН ₃ — СН ₃ — ОН	3-[BUTYRYL-(3-METHYL-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
447	CI CH ₃	3-[BUTYRYL-(2-CHLORO-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
448	H ₃ C CH ₃ CH ₃ CH ₃	3-[ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5- #MI-TOLYL-THIOPHENE-2-CARBOXYLIC ACID	· +++
449	CI CH ₃ CH ₃ CH ₃	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-THIAZOL-2-YL- THIOPHENE-2-CARBOXYLIC ACID	* * *
450	о сн,	3-(ACETYL-BENZYL-AMINO)-5-PHENYL-	
451	CH _s	THIOPHENE-2-CARBOXYLIC ACID 3-(BENZYL-PROPIONYL-AMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
452	O CH ₃	3-[BENZYL-(2-METHOXY-ACETYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
453	O CH ₃ CH ₃ OH	3-[BENZYL-(3-METHYL-BUTYRYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
454	S OH	3-(BENZYL-CYCLOPROPANECARBONYL- AMINO)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
455		3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
456	~	3-[(4-CHLORO-BENZYL)-PROPIONYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	, +++

	MOLSTRUCTURE	COMPOUND NAME	IC50
457	CH _S CH _S OH	3-[(4-CHLORO-BENZYL)-ISOBUTYRYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
458	CI O CH ₃ CH ₃ OH	3-[(4-CHLORO-BENZYL)-(3-METHYL- BUTYRYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
459	CI N N OH	3-[(4-CHLORO-BENZYL)- CYCLOPROPANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
460	H ₃ C CH ₃ CH ₃ OH	5-(4-ACETYL-PHENYL)-3-[ISOPROPYL-(4- METHYL-CYCLOHEXANECARBONYL)- AMINO]-THIOPHENE-2-CARBOXYLIC	+++
461		3-[(4-CHLORO-BENZYL)- CYCLOBUTANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
462	CH _N CH ₃	3-[BUTYRYL-(4-CHLORO-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
463	CI N N OH	3-[(4-CHLORO-BENZYL)-(2- CYCLOPENTYL-ACETYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
464	FF F CH ₃	3-[ACETYL-(4-TRIFLUOROMETHYL- BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	
465	CH _s OCH _s CH _s OCH	3-[ISOBUTYRYL-(3-METHYL-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2-	++
. 466		3-[CYCLOPROPANECARBONYL-(3- METHYL-BENZYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	

	MOLSTRUCTURE	COMPOUND NAME	IC50
467	СН,	3-[(4-METHYL-BENZYL)-PROPIONYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
468	CH ₃ CH ₃ CH ₃ OH	3-[ISOBUTYRYL-(4-METHYL-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
469	CH, OH	3-[CYCLOPROPANECARBONYL-(4- METHYL-BENZYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
470	CH, N CH, S OH	3-[BUTYRYL-(4-METHYL-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
471		3-[(3-METHOXY-BENZYL)-PROPIONYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+

	MOLSTRUCTURE	COMPOUND NAME	IC50
472	CMe CH ₃ CH ₃ CH ₃	3-[(3-METHOXY-BENZYL)-(3-METHYL- BUTYRYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
473	SMe SMe OH	3-[CYCLOBUTANECARBONYL-(3- METHOXY-BENZYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	-11-
474	H ₃ C CH ₃ CH ₃ NH ₂ OH	3-[(2-CARBAMOYL-4-METHYL-BENZOYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
475	S OH	3-[BUTYRYL-(3-METHOXY-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
476	~	3-[ACETYL-(3-CHLORO-BENZYL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+

	MOLSTRUCTURE	COMPOUND NAME	IC50
477	сн,	3-[(3-CHLORO-BENZYL)-PROPIONYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
478	CI O CH ₃ OH	3-[(3-CHLORO-BENZYL)-(2-METHOXY- ACETYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	
479	CI CH ₃ CH ₃	3-[(3-CHLORO-BENZYL)-(3-METHYL- BUTYRYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
480		3-[(3-CHLORO-BENZYL)- CYCLOPROPANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC	++
481	OH OH	3-[(3-CHLORO-BENZYL)- CYCLOBUTANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
482	CI OCH, OCH,	3-[BUTYRYL-(3-CHLORO-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
483	F CH ₃ OH	3-[ACETYL-(2,4-DIFLUORO-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
484	~ .	3-[(2,4-DIFLUORO-BENZYL)-(2-METHOXY- ACETYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	++
485	~	3-[(2,4-DIFLUORO-BENZYL)- ISOBUTYRYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
486		3-[(2,4-DIFLUORO-BENZYL)-(3-METHYL- BUTYRYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	

	MOLETPHOTUPE	· · · · · · · · · · · · · · · · · · ·	CT/CA02/00
<u></u>	MOLSTRUCTURE	COMPOUND NAME	IC50
487	- NOH	3-[BENZYL-(2-CYCLOPENTYL-ACETYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
488	CI CH, CH, SH,	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-(1H-INDOL-5-YL)- THIOPHENE-2-CARBOXYLIC ACID	+++
489	S OH	3-(BENZYL-CYCLOBUTANECARBONYL- AMINO)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	
490	F OH	3-[CYCLOHEXANECARBONYL-(2,4- DIFLUORO-BENZYL)-AMINO]-5-PHENYL-	+++
491	H ₃ C-O O=CH ₂ SOOH	3-{ALLYL-[2-(4-METHOXY-PHENYL)- ACETYL]-AMINO}-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID	+

	MOLSTRUCTURE	COMPOUND NAME	IC50
492	H ₃ C O= O= OCH ₃ OH	3-(ETHYL-HEXANOYL-AMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
493	CH ₃ O= CH ₃ OH	3-(BUTYRYL-ETHYL-AMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
494	H ₃ C CH ₃ O CH ₃ O H	3-[ETHYL-(4-METHYL-PENTANOYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
495	~	3-[CYCLOBUTANECARBONYL-(2,4- DIFLUORO-BENZYL)-AMINO]-5-PHENYL-	+++
496	F CH ₃	3-[BUTYRYL-(2,4-DIFLUORO-BENZYL)- AMINO]-5-PHENYL-THIOPHENE-2-	++ +

	MOLSTRUCTURE	COMPOUND NAME	1050
	WOLSTRUCTURE	COMPOUND NAME	IC50
497	N-CH ₃	3-(CYCLOPENTANECARBONYL-METHYL- AMINO)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
498	ON-CH ₃ OH	3-(CYCLOHEXANECARBONYL-METHYL- AMINO)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++ +
499	H ₃ C CH ₃ H ₃ C O O O O O O O O O O O O O O O O O O O	3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(2,4-DICHLORO-BENZOYL)-AMINO]- PYRROLIDINE-1-CARBOXYLIC ACID #TERTI-BUTYL ESTER	
500	H ₃ C CH ₃ CH ₃ OH	3-[(1,4-DIMETHYL- CYCLOHEXANECARBONYL)-ISOPROPYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
· 501	H ₃ C CH ₃ OH	5-(4-ETHYL-PHENYL)-3-[(2-HYDROXY-4- METHYL-BENZOYL)-ISOPROPYL-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
,	- CH ₃ OH		
502	СН	3-[(2-HYDROXY-4-METHYL-BENZOYL)- ISOPROPYL-AMINO]-5-#M!-TOLYL- THIOPHENE-2-CARBOXYLIC ACID	+++
	СІН		
503	N CI S OH	3-[(2,4-DICHLORO-BENZOYL)- PYRROLIDIN-3-YL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
	CH ₃	·	
504		4-{5-CARBOXY-4-[(2,4-DICHLORO- BENZOYL)-ISOPROPYL-AMINO]- THIOPHEN-2-YL}-3,6-DIHYDRO-2#H!- PYRIDINE-1-CARBOXYLIC ACID BENZYL ESTER	+++
		3-{[2-(HYDROXYIMINO-METHYL)-4-	
505		METHYL-BENZOYL]-ISOPROPYL-AMINO}- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
506	S' Fon	3-[(1-CARBAMIMIDOYL-PIPERIDIN-4-YL)- (2,4-DICHLORO-BENZOYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	

	MOLSTRUCTURE	COMPOUND NAME	IC50
	н,с сн, о сн,		
507	N C C C C C C C C C C C C C C C C C C C	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(2,4-DICHLORO-BENZOYL)-AMINO]- AZEPANE-1-CARBOXYLIC ACID TERT!- BUTYL ESTER	+++
508	CI NOOH	4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(2,4-DICHLORO-BENZOYL)-AMINO]- METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER	+++
	ан	·	
509	S OH	3-[AZEPAN-4-YL-(2,4-DICHLORO- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
510		3-[(4-METHYL- CYCLOHEXANECARBONYL)-PIPERIDIN- 4-YL-AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID LITHIUM SALT	++
511	J 's' J	3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(2,4-DICHLORO-BENZOYL)-AMINO]- PIPERIDINE-1-CARBOXYLIC ACID #TERTI-BUTYL ESTER	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
512	The state of the s	3-[(4-BENZYLOXYCARBONYLAMINO- CYCLOHEXYL)-(2,4-DICHLORO- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
513	H ₃ C CH ₃ CH ₃	3-[ISOPROPYL-(4-METHYL-2-OXO- CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
514	CI NH CI OH OH	3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN- 3-YL-AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID; COMPOUND WITH GENERIC INORGANIC NEUTRAL COMPONENT	+++
515	a Control	3-[(4-BENZYLOXYCARBONYLAMINO- CYCLOHEXYL)-(2,4-DICHLORO- BENZOYL)-AMINO]-5-PHENYL-	+++
516	CI CI O O O O O O O O O O O O O O O O O	3-[(2-BENZYLOXY-1-METHYL-ETHYL)- (2,4-DICHLORO-BENZOYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC	+++
517	s	3-[(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-(4- METHYL-CYCLOHEXANECARBONYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
518	HO — NO CI	3-[(2,4-DICHLORO-BENZOYL)-(2- HYDROXY-1-HYDROXYMETHYL-ETHYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
519	HN CH CH	3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN- 4-YLMETHYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
520	HN CI S OH	3-[(2-CHLORO-BENZOYL)-PIPERIDIN-4- YLMETHYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
521	H ₃ C NH OO OH	3-[(4,6-DICHLORO-1#H!-INDOLE-2- CARBONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	· +++
522	H ₃ C OH CI	3-[(2,4-DICHLORO-BENZOYL)-(2- HYDROXY-1-METHYL-ETHYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC	+++
523	s' s' l'	4-{1-[(2-CARBOXY-5-PHENYL-THIOPHEN- 3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]- ETHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
524	H ₃ C CH ₃ OH OH	4-{5-CARBOXY-4-{ISOPROPYL-(4- METHYL-CYCLOHEXANECARBONYL}- AMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO- 2#H!-PYRIDINE-1-CARBOXYLIC ACID BENZYL ESTER	+++
525	CH ₃	3-[(4-METHYL- CYCLOHEXANECARBONYL)-PYRIDIN-4- YL-AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
	a l		
526	FF OH	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-5-PIPERIDIN-4-YL- THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID	+
	H ₃ C,CH ₃		
527	S OH CH ₃	3-[ISOPROPYL-(4-PROPYL- CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
528	OH FFO	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(2,4-DICHLORO-BENZOYL)-AMINO]- CYCLOHEXYL-AMMONIUM; TRIFLUORO- ACETATE	+++
529	. Обрания	3-[(2,4-DICHLORO-BENZOYL)-(1- PIPERIDIN-4-YL-ETHYL)-AMINO]-5- PHENYL-THIOPHENE-2- CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
		COM COND NAME	1030
	H ₃ C-N-OH	3-[(CYCLOHEX-3-ENECARBONYL)- ISOPROPYL-AMINO]-5-PHENYL-	
530		THIOPHENE-2-CARBOXYLIC ACID	++
531	H ₃ C CH ₃ CH ₃ CH ₃	3-[(4-ETHYL-CYCLOHEXANECARBONYL)- ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
532	CI CH ₃ OH	3-[(4-CHLORO- CYCLOHEXANECARBONYL)-ISOPROPYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
533	H ₃ C N CI CI OH	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-3- METHYL- PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER	+++
534	H ₃ C-O N CI OH	3-[(2,4-DICHLORO-BENZOYL)-(2- METHOXY-CYCLOHEXYL)-AMINO]-5- PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
535		3-[(2,4-DICHLORO-BENZOYL)-(2,2- DIMETHYL-[1,3]DIOXAN-5-YL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++

	MOLSTRUCTURE COMPOUND NAME		C1/CA02/00
-	WIOLSTRUCTURE	COMPOUND NAME	IC50
536	H ₃ C-N CH ₃	3-[ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5-(1- METHYL-PIPERIDIN-4-YL)-THIOPHENE-2- CARBOXYLIC ACID	+++
537	F OH H _s C OH OH	3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL- PIPERIDIN-4-YL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID	+++
538	HO N CI	3-[(2,4-DICHLORO-BENZOYL)-(2- HYDROXY-CYCLOHEXYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC AÇID	+++
539	C S TOH	4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]- METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER	+++
540	S To	3-[((1R,2S,4R)-2-HYDROXY-4-METHYL- CYCLOHEXANECARBONYL)-ISOPROPYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
541	H,C CH, N CH, CH, O CH, O CH, O CH,	3-{ISOPROPYL-[1-(4-METHOXY-2,3,6- TRIMETHYL-BENZENESULFONYL)-5- METHYL-1,2,3,6-TETRAHYDRO- PYRIDINE-2-CARBONYLJ-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
			1
542	CH, CI CI S OH	3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-4-FLUORO-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
	CiH		
	H ₃ C ₁	·	
	STOH	3-[(2,4-DICHLORO-BENZOYL)-(1-METHYL-	•
543		PIPERIDIN-4-YL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	++
	F-NO-CH,	4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-	
544		METHYL}-PIPERIDINIUM; TRIFLUORO- ACETATE	+++
545	\$ 500	3-[(2-TERT-BUTOXYCARBONYLAMINO-1- METHYL-ETHYL)-(2,4-DICHLORO- BENZOYL)-AMINO]-5-PHENYL-	+++
-	0		
546		2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(2,4-DICHLORO-BENZOYL)-AMINO]- PROPYL-AMINE TRIFLUOROACETIC ACID SALT	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
	0	COME MAIL	
547	HO-N	3-[(3-CARBOXY-CYCLOPENTYL)-(2,4- DICHLORO-BENZOYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
	$^{\circ}$		
548	0 0	3-[(3-CARBOXY-CYCLOPENTYL)-(2,4- DICHLORO-BENZOYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
	1		
549	~	2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-Y L)-(2,4-DICHLORO-BENZOYL)-AMINO]-CY CLOHEXYL-AMMONIUM; CHLORIDE	+++
550	N-CH _s	3-(BENZOYL-METHYL-AMINO)-5-PHENYL-	
550	CH ₃	THIOPHENE-2-CARBOXYLIC ACID	+
551	O=s=O NH S HOH	{[5-PHENYL-3-(TOLUENE-4- SULFONYLAMINO)-THIOPHENE-2- CARBONYL]-AMINO}-ACETIC ACID	++
552	BC S OH CH ₃	5-BROMO-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2-	++

	MOLSTRUCTURE	COMPOUND NAME	IC50
553	OH OH	3-[CYCLOHEXYL-(2,4-DICHLORO- BENZOYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	- - - -
554	ON CH ₃	3-[[1,3]DIOXAN-5-YL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
555	STOHLO	3-[[2-(TERT-BUTYL-DIMETHYL- SILANYLOXY)-1-METHYL-2-PHENYL- ETHYL]-(2,4-DICHLORO-BENZOYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	
556	J's T	3-[[2-(TERT-BUTYL-DIMETHYL- SILANYLOXY)-1-METHYL-2-PHENYL- ETHYL]-(2,4-DICHLORO-BENZOYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++
557		3-[(2,4-DICHLORO-BENZOYL)-(2- DIETHYLAMINO-THIAZOL-5-YLMETHYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	***
558		(5-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3- YL)-(2,4-DICHLORO-BENZOYL)-AMINO]- METHYL}-THIAZOL-2-YL)-DIETHYL- AMMONIUM; CHLORIDE	+++

	D 02/100851 PC		
	MOLSTRUCTURE	COMPOUND NAME	IC50
559	H ₃ C CH ₃ CH ₃	5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4- METHYL-CYCLOHEXANECARBONYL)- AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
	CH _{chiral}		
560	H ₃ C CH ₃ OH	3-[((1S,2R,4S)-2-HYDROXY-4-METHYL- CYCLOHEXANECARBONYL)-ISOPROPYL- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
561	H ₃ C CH ₃	3-[(2,4-DICHLORO-BENZOYL)-(2- METHOXY-1-METHYL-ETHYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
562	s "	3-[(4S)-ISOPROPYL-(4-METHYL- CYCLOHEX-1-ENECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	· +++
563	O NH ₂ O=S CH ₃	5-(4-CHLORO-PHENYL)-3-(TOLUENE-4- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID AMIDE	++
564	Ŭ	5-(4-FLUORO-PHENYL)-3-(TOLUENE-4- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID AMIDE	++

	MOLSTRUCTURE COMPOUND NAME		C1/CA02/00
	WICLSTRUCTURE	COMPOUND NAME	IC50
	H ₃ C ^O NH ₂ - O ₂ S ^O NH H ₃ C	5-'(4-METHOXY-PHENYL)-3-(TOLUENE-4- SULFONYLAMINO)-THIOPHENE-2-	
565		CARBOXYLIC ACIÓ AMIDE	++
EGG	CH ₃ N S O O O O O O O O O O O O O O O O O O	3-METHYL-(4-METHYLBENZOYL)- AMINO)5-PHENYL THIOPHENE-2- CARBOXYLIC ACID (2-HYDROXY-	
566		ETHYL)AMIDE	++
567	S HN CH _s	5-PHENYL-3-(TOLUENE-4- SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID CYCLOBUTYLAMIDE	++
568	Н ₃ С О СН ₃	3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID AMIDE	++
	,ci ı		
569	H ₃ C-NOO CI	5-BROMO-3-[(2,4-DICHLORO-BENZOYL)- ISOPROPYL-AMINO]-THIOPHENE-2- CARBOXYLIC ACID	+++
	H ₃ C CH ₃ CH ₃	5-(4-CHLORO-PHENYL)-3-[ISOPROPYL-(4- METHYL-CYCLOHEXANECARBONYL)- AMINO]-THIOPHENE-2-CARBOXYLIC	
570		4 5 5	+++

_wo	02/100851	P	CT/CA02/00876
	MOLSTRUCTURE	COMPOUND NAME	IC50
571	H,C-CH,OH	5-(4'-CHLORO-BIPHENYL-4-YL)-3- [ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	+++
572	S OH	3-[(4-METHYL- CYCLOHEXANECARBONYL)- (TETRAHYDRO-PYRAN-4-YL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	+++
573	ö	3-[(4-METHYL- CYCLOHEXANECARBONYL)-(1-METHYL- PIPERIDIN-4-YL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	+++
574	N O CH ₃	3-[(4-METHYL- CYCLOHEXANECARBONYL)-PIPERIDIN- 4-YL-AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+
575	H ₃ C CH ₃ BH	'3-[ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5-(4- TRIFLUOROMETHYL-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID	+++
576	n ₃ C 7	5-(4-CYANO-PHENYL)-3-[ISOPROPYL-(4- METHYL-CYCLOHEXANECARBONYL)- AMINO]-THIOPHENE-2-CARBOXYLIC ACID	+++
577	H ₃ C N	'3-[ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5-(4- METHOXY-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID	+++

	MOLSTRUCTURE	COMPOUND NAME	IC50
578	н,с о-сн, сн,	3-[(2-METHOXY-1-METHYL-ETHYL)-(4- METHYL-CYCLOHEXANECARBONYL)- AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
579	о содн	3-[CYCLOHEXYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
580	O S N N	3-(4-CHLORO-2,5 DIMETHYL- BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE2-CARBOXYLIC ACID AMIDE	+++
583		3-[(2,4-DICHLORO-PHENYL)-ISOPROPYL- CARBAMOYL]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	+++
584		3-(METHYL-P-TOLYL-CARBAMOYL)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	++
585		3-[(2,4-DICHLORO-PHENYL)-METHYL- CARBAMOYL]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	++

*: +++ IC₅₀ <5μM

++ IC₅₀ 5μM-20μM

+ $IC_{50} > 20 \mu M$

5

EXAMPLE 28 List of compounds having anti-helicase activity *

Compound	Compound name	Structure	Anti-	Anti-
#			ATPase	ATPase
				(HPLC
			(Malachite	method)
			Green	EC ₅₀
			assay)	
			EC _{so}	
Compound	3-(4-Chloro-2,5-	√ CI	+	ND
#14	dimethyl-	18		
	benzenesulfonylamin	S CO ₂ H		
	o)-5-(4-chloro-	cr Cr		
	phenyl)-thiophene-			
	2-carboxylic acid			
Compound	3-(4-Chloro-2,5-	CI	+++	++
#19	dimethyl-			
	benzenesulfonylamin	СО _Р Н		
	o)-5-(4-isobutyl-			
	phenyl)-thiophene-			
}	2-carboxylic acid			
			ςΩ	
Compound	3-(4-Bromo-2-	B '	ND	+++
#223	fluorobenzenesulfo-	[
	nylamino)-5-(4-	OF NH		
	isobutylphenyl)-	CH, CHS		
}	thiophene-2-	н,с		,
	carboxylic acid			
Compound	3-(4-Bromo-2-	Br	ND	++
#224	methylbenzenesulfo-	H ₃ C—		
ŀ	nylamino)-5-(4-	O'S NH		
1	isobutylphenyl)-	OH OH		
	thiophene-2-	H _C CH ₃ S		
	carboxyric acid			
Compound	5-(4-Isobutylphenyl	~}	ND	+
#225	3-(3-methoxy-	. 🔎		
	benzenesulfonyl-	O'S NH	·	
	amino)-thiophene-2-	OH	Ì	
	carboxylic acid	H _C CH ₃ S		
L				

			FC1/CA	
Compound	5-(4-Isobutyl-	F	ND	++
#581	phenyl)-3-[5-(5-	₽ F		
	trifluoromethyl-	"\		
	isoxazol-3-yl)-	\$		
-	thiophene-2-	O,S NH		
	sulfonylamino]-	ОН		
1	thiophene-2-	CH, S		
	carboxylic acid	ңс		
Compound	3-[2,5-Bis-(2,2,2-	F,F	ND	+
#227	trifluoroethoxy)-			
	benzenesulfonylamin	O'S NH		
	o]-5-(4-isobutyl-	CH, S		
	phenyl)-thiophene-	ң _с		
	2-carboxylic acid		·	
Compound	3-(2-Chloro-4-	// ^N	ND	+
#228	cyanobenzenesulfony			
ļ	lamino)-5-(4-	, <u></u>		
	isobutylphenyl)-	ON HO.		
]	thiophene-2-	CH CHS		
	carboxylic acid	н,с		
Compound	5-(4-Isobutyl-	F	ND	+
#582	phenyl)-3-(2,3,4-	F		
	trifluoro-	0, S F		
	benzenesulfonylamin	O, NH		
	o)-thiophene-2-	CH. S		
	carboxylic acid	H _s c ·		
L	l			1

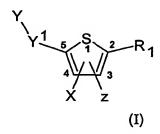
*: +++ $IC_{50} < 5\mu M$

++ IC₅₀ 5μM-20μM

+ IC₅₀ >20µM

We claim:

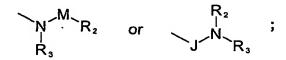
1. A compound having the formula I:



or pharmaceutically acceptable salts thereof;

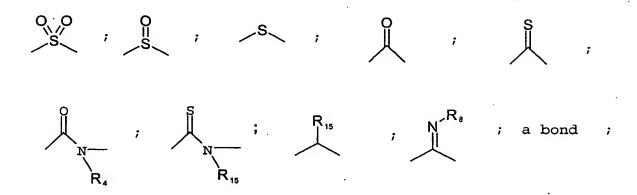
wherein,

X is chosen from:



wherein,

M is chosen from:

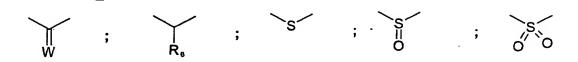


wherein,

R₄ is C ₁₋₆ alkyl;

 R_8 is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-16}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R_{15} is chosen from H or C $_{1-6}$ alkyl;

J is chosen from:



wherein, W is chosen from O, S or NR,

wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{12}$ alkynyl, C $_{6-16}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl;

and R_6 is chosen from H, C $_{1-12}$ alkyl, C $_{6-14}$ aryl or C $_{6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{2}OR_{5}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1\text{-}12}$ alkyl, C $_{2\text{-}12}$ alkenyl, C $_{2\text{-}12}$ alkynyl, C $_{6\text{-}14}$ aryl, C $_{3\text{-}12}$ heterocycle, C $_{3\text{-}18}$ heteroaralkyl and C $_{6\text{-}18}$ aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{4-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl and C $_{4-18}$ aralkyl; provided that R_{16} is other than methyl or ethyl;

 R_1 is chosen from C $_{2-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl or C $_{6-18}$ aralkyl;

 $\rm R_2$ is chosen from C $_{2-12}$ alkyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl, or C $_{6-18}$ aralkyl;

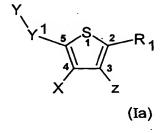
 R_3 is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl or C $_{6-18}$ aralkyl;

Z is chosen from H, halogen, C₁₋₆ alkyl;

with the proviso that:

i) when X is 4-Chloro-2,6-dimethyl-benzenesulfonamide and, R_1 is phenyl, and R_3 is H, and Y is a bond, then Y is other than CONH₂; compound #580

- ii) when X is Toluene-4-sulfonamide and R_1 is 4-chlorophenyl, and R_3 is H, and Y is a bond, then Y is other than CONH,; compound #563
- iii) when X is Toluene-4-sulfonamide and R_1 is 4-fluorophenyl, and R_3 is H, and Y is a bond, then Y is other than CONH₂; compound #564
- iv) when X is Toluene-4-sulfonamide and R_1 is 4-methoxy-phenyl, and R_3 is H, and Y¹ is a bond, then Y is other than CONH₂; compound #565
- v) when X is Benzamide and R_1 is phenyl Y^1 is a bond and Y is COOH then R_3 is other than hydrogen.
- 2. A compound having the formula Ia:



or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N_{R_3}^{M}$$
 or $N_{R_3}^{R_2}$;

wherein,

M is chosen from:

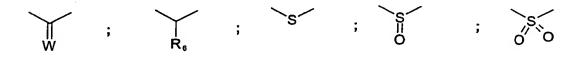
$$R_4$$
, R_{15}

wherein,

R, is C 1-6 alkyl;

 $\rm R_8$ is chosen from H, C $_{1\text{-}12}$ alkyl, C $_{2\text{-}12}$ alkenyl, C $_{2\text{-}12}$ alkynyl, C $_{6\text{-}14}$ aryl, C $_{3\text{-}12}$ heterocycle, C $_{3\text{-}12}$ heteroaralkyl, C $_{6\text{-}16}$ aralkyl; and R $_{15}$ is chosen from H or C $_{1\text{-}6}$ alkyl;

J is chosen from:



wherein W is chosen from O, S or NR,

wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-14}$ aralkyl;

and R_{ϵ} is chosen from H, C $_{1-12}$ alkyl, C $_{6-14}$ aryl or C $_{6-16}$ aralkyl;

Y is chosen from a bond, C₁₋₆ alkyl, C ₂₋₆ alkenyl or C ₂₋₆ alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{2}OR_{5}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{3-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl and C $_{6-18}$ aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl; provided that R_{16} is other than methyl or ethyl;

 R_1 is chosen from C $_{2-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-16}$ heteroaralkyl or C $_{6-18}$ aralkyl;

 R_2 is chosen from C $_{2-12}$ alkyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, or C $_{6-18}$ aralkyl;

 R_3 is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl or C $_{6-18}$ aralkyl;

Z is chosen from H, halogen, C1-6 alkyl;

with the proviso that:

i) when X is 4-Chloro-2,6-dimethyl-benzenesulfonamide and, R_1 is phenyl, and R_3 is H, and Y is a bond, then Y is other than CONH,; compound #580

ii) when X is Toluene-4-sulfonamide and R_i is 4-chlorophenyl, and R_i is H, and Y is a bond, then Y is other than CONH,; compound #563

- iii) when X is Toluene-4-sulfonamide and R_1 is 4-fluorophenyl, and R_3 is H, and Y is a bond, then Y is other than CONH₂; compound #564
- iv) when X is Toluene-4-sulfonamide and R_1 is 4-methoxy-phenyl, and R_3 is H, and Y is a bond, then Y is other than CONH2; compound #565
- v) when X is Benzamide and R1 is phenyl Y1 is a bond and Y is COOH then R3 is other than hydrogen.
- 3. A compound as defined in claims 1 or 2, wherein X is:

4. A compound as defined in claims 1 or 2, wherein

X is:

- 5. The compound as defined in claims 1 or 2, wherein Z is H.
- 6. The compound as defined in claims 1 or 2, wherein Y is a bond.
- 7. The compound as defined in anyone of claims 1 or 2, wherein R_1 is chosen from C_{2-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl.

8. The compound as defined in anyone of claims 1 or 2, wherein R_1 is chosen from a C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle.

- 9. The compound as defined in anyone of claims 1 or 2, wherein R_1 is a C_{2-12} alkyl.
- 10. The compound as defined in anyone of claims 1 or 2, wherein R_1 is a C_{6-14} aryl.
- 11. The compound as defined in anyone of claims 1 or 2, wherein R_1 is a C_{3-12} heterocycle.
- 12. The compound as defined in anyone of claims 1 or 2, wherein R₁ is chosen from t-butyl, isobutyl, allyl, ethynyl, 2-phenylethenyl, isobutenyl, benzyl, phenyl, phenethyl, benzodioxolyl, thienyl, thiophenyl, pyridinyl, isoxazolyl, thiazolyl, pyrazolyl, tetrazolyl, benzofuranyl, indolyl, furanyl, or benzothiophenyl any of which can be optionally substituted by one or more substituent chosen from halogen, nitro, nitroso, SO3R12, PO3RCRd, CONR13R14, COOH, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C6-12 aralkyl, C6-12 aryl, C1-6 alkyloxy, C2-6 alkenyloxy, C2-6 alkynyloxy, C6-12 aryloxy, C(0)C1-6 alkyl, C(0)C2-6 alkenyl, C(0)C2-6 alkynyl, C(0)C6-12 aryl, C(0)C6-12 aralkyl, C3-10 heterocycle, hydroxyl, NR13R14, C(0)OR12, cyano, azido, amidino or guanido;

wherein R_{12} , Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

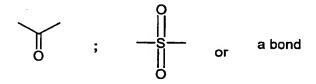
- or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
- or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

13. The compound as defined in claim 12, wherein R₁ is chosen from thienyl, t-butyl, phenyl or pyridinyl.

- 14. The compound as defined in claim 12, wherein R_1 is phenyl.
- 15. The compound as defined in anyone of claims 1 or 2, wherein R_i is phenyl substituted by at least one fluoride.
- 16. The compound as defined in anyone of claims 1 or 2, wherein R_i phenyl substituted by at least one chloride.
- 17. The compound as defined in anyone of claims 1 or 2, wherein R_1 is phenyl substituted by at least one nitro.
- 18. The compound as defined in anyone of claims 1 or 2, wherein R₁ is phenyl substituted by at least one methyl.
- 19. The compound as defined in anyone of claims 1 or 2, wherein R_1 phenyl substituted by at least one methoxy.
- 20. The compound as defined in anyone of claims 1 or 2, wherein R_1 is thienyl.
- 21. The compound as defined in anyone of claims 1 or 2, wherein R is thienyl substituted by at least one halogen.
- 22. The compound as defined in anyone of claims 1 or 2, wherein R_i is thienyl substituted by at least one chloride.
- 23. The compound as defined in anyone of claims 1 or 2, wherein R_1 is thienyl substituted by at least one methyl.

24. The compound as defined in anyone of claims 1 or 2, wherein R_1 is thienyl substituted by at least one methyl and one chloride.

- 25. The compound as defined in anyone of claims 1 or 2, wherein R is isoxazolyl substituted by at least one methyl.
- 26. The compound as defined in anyone of claims 1 or 2, wherein R_i is pyridinyl.
- 27. The compound as defined in anyone of claims 1 or 2, wherein M is chosen from:



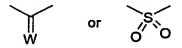
28. The compound as defined in anyone of claims 1 or 2, wherein M is:



29. The compound as defined anyone of claims 1 or 2, wherein M is:



30. The compound as defined in anyone of claims 1 or 2, wherein J is chosen from:



wherein W is as defined in claim 1.

31. The compound as defined in anyone of claims 1 or 2, wherein J is:



32. The compound as defined in anyone of claims 1 or 2, wherein J is:



- 33. The compound as defined in anyone of claims 1 or 2, wherein Y is chosen from COOR₁₆, COCOOR₅, P(O)OR₂OR₅, S(O)₂OR₅, tetrazole, CON(R₅)CH(R₅)COOR₅, CONR₁₀R₁₁, CONR₂OH.
- 34. The compound as defined in claim 33, wherein any of R_s , Ra, Rb, R_9 , R_{10} , R_{11} and R_{16} are each independently chosen from H or C_{1-6} alkyl; provided that R_{16} is other than methyl or ethyl.
- 35. The compound as defined in anyone of claims 1 or 2, wherein Y is chosen from $COOR_{16}$, $CONR_{10}R_{11}$ or $CON(R_9)CH(R_5)-COOR_5$.
- 36. The compound as defined in claim 33, wherein any of R_5 , R_9 , R_{10} , R_{11} and R_{16} are each independently chosen from H or C_{1-6} alkyl; provided that R_{16} is other than methyl or ethyl.
- 37. The compound as defined in anyone of claims 1 or 2, wherein Y is COOH.

38. The compound as defined in anyone of claims 1 or 2, wherein Y is CONHCH, COOH.

- 39. The compound as defined in anyone of claims 1 or 2, wherein Y is COOCH.
- 40. The compound as defined in anyone of claims 1 or 2, wherein Y is COONH,.
- 41. The compound as defined in anyone of claims 1 or 2, wherein R_3 is chosen from H, C_{1-12} alkyl, C_{6-18} aralkyl, C_{3-12} heterocycle or C_{3-18} heteroaralkyl.
- 42. The compound as defined in anyone of claims 1 or 2, wherein R_3 is chosen from H, C_{1-12} alkyl, C_{6-18} aralkyl or C_{3-12} heterocycle.
- 43. The compound as defined in anyone of claims 1 or 2, wherein R_3 is C_{1-12} alkyl.
- 44. The compound as defined in anyone of claims 1 or 2, wherein R_3 is C_{6-18} aralkyl.
- 45. The compound as defined in anyone of claims 1 or 2, wherein R_3 is C_{3-12} heterocycle.
- 46. The compound as defined in anyone of claims 1 or 2, wherein R₃ is chosen from H, methyl, ethyl, i-propyl, cyclopropyl, cyclohexyl, allyl, piperidinyl, piperazinyl, pyrrolidinyl, azetidinyl, aziridinyl, pyridinyl, piperidinylmethyl, dioxanyl, azepanyl or benzyl; any of which can be optionally substituted by one or more substituent chosen from halogen, nitro, nitroso, SO₃R₁₂, PO₃RcRd, CONR₁₃R₁₄, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₂₋₆ alkenyloxy,

 C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(0)C_{1-6}$ alkyl, $C(0)C_{2-6}$ alkenyl, $C(0)C_{2-6}$ alkynyl, $C(0)C_{6-12}$ aryl, $C(0)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(0)OR_{12}$, cyano, azido, amidino or guanido; wherein R_{12} , Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl; or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle; or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

- 47. The compound as defined in claim 43, wherein R₃ is chosen from H or Methyl, isopropyl, piperidinyl, piperidinylmethyl or cyclohexyl.
- 48. The compound as defined in anyone of claims 1 or 2, wherein R_3 is H.
- 49. The compound as defined in anyone of claims 1 or 2, wherein R_3 is Methyl.
- 50. The compound as defined in anyone of claims 1 or 2, wherein R_{2} is C_{2-12} alkyl, C_{6-14} aryl or C_{3-12} heterocycle.
- 51. The compound as defined in anyone of claims 1 or 2, wherein R_2 is C_{3-6} heterocycle.
- 52. The compound as defined in anyone of claims 1 or 2, wherein R₂ is chosen from thienyl, furanyl, pyridinyl, oxazolyl, thiazolyl, pyrrolyl, benzofuranyl, indolyl, benzoxazolyl, benzothienyl, benzothiazolyl, piperazinyl, pyrrolidinyl or quinolinyl any of which can be optionally substituted by one or more substituent chosen from halogen, nitro, nitroso, SO₃R₁₂, PO₃RcRd, CONR₁₃R₁₄, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₆₋₁₂

aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} -aryloxy, $C(0)C_{1-6}$ alkyl, $C(0)C_{2-6}$ alkenyl, $C(0)C_{2-6}$ alkynyl, $C(0)C_{6-12}$ aryl, $C(0)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(0)OR_{12}$, cyano, azido, amidino or guanido; wherein R_{12} , Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-16} heteroaralkyl, C_{6-16} aralkyl; or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle; or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

- 53. The compound as defined in claim 49, wherein R₂ is a heterocycle chosen from thienyl, furanyl, pyridinyl, pyrrolyl, indolyl, piperazinyl or benzothienyl.
- 54. The compound as defined in anyone of claims 1 or 2, wherein R_2 is C_{2-12} alkyl.
- 55. The compound as defined in anyone of claims 2 to 4, wherein R₂ is chosen from cyclopropyl, cyclobutyl, cyclopentyl, cyclopentyl, cyclopentyl, cyclopentyl, cyclopentyl, cyclopentyl, 2-(cyclopentyl)-ethyl, methyl, ethyl, vinyl, propyl, propenyl, isopropyl, butyl, butenyl isobutyl, pentyl, neopentyl or t-butyl any of which can be optionally substituted by one or more substituent chosen from halogen, nitro, nitroso, SO₃R₁₂, PO₃RcRd, CONR₁₃R₁₄, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, C₆₋₁₂ aryloxy, C(O)C₁₋₆ alkyl, C(O)C₂₋₆ alkenyl, C(O)C₂₋₆ alkynyl, C(O)C₆₋₁₂ aryl, C(O)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, NR13R14, C(O)OR₁₂, cyano, azido, amidino or guanido;

wherein R_{12} , Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

- or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
- or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
- 56. The compound as defined in anyone of claims 1 or 2, wherein R_2 is C_{6-12} aryl.
- 57. The compound as defined in anyone of claims 1 or 2, wherein R, is an aryl chosen from indenyl, naphthyl or biphenyl.
- 58. The compound as defined in anyone of claims 2 to 4, wherein R₂ is phenyl substituted by one or more substituent chosen from halogen, nitro, nitroso, SO₃R₁₂, PO₃RCRd, CONR₁₃R₁₄, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₆₋₁₂ aralkyl, C₆₋₁₂ aryl, C₁₋₆ alkyloxy, C₂₋₆ alkenyloxy, C₂₋₆ alkynyloxy, C₆₋₁₂ aryloxy, C(0)C₁₋₆ alkyl, C(0)C₂₋₆ alkenyl, C(0)C₂₋₆ alkynyl, C(0)C₆₋₁₂ aryl, C(0)C₆₋₁₂ aralkyl, C₃₋₁₀ heterocycle, hydroxyl, NR₁₃R₁₄, C(0)OR₁₂, cyano, azido, amidino or guanido;

wherein R_{12} , Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{4-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

- or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
- or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
- 59. The compound as defined in anyone of claims 1 or 2, wherein R is phenyl substituted by one or two substituents chosen from

halogen, nitro, nitroso, SO_3R_{12} , PO_3RCRd , $CONR_{13}R_{14}$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-12} aralkyl, C_{6-12} aryl, C_{1-6} alkyloxy, C_{2-6} alkenyloxy, C_{2-6} alkynyloxy, C_{6-12} aryloxy, $C(0)C_{1-6}$ alkyl, $C(0)C_{2-6}$ alkenyl, $C(0)C_{2-6}$ alkynyl, $C(0)C_{6-12}$ aryl, $C(0)C_{6-12}$ aralkyl, C_{3-10} heterocycle, hydroxyl, $NR_{13}R_{14}$, $C(0)OR_{12}$, cyano, azido, amidino or guanido;

wherein R_{12} , Rc, Rd, R_{13} and R_{14} are each independently chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{4-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{4-18} aralkyl;

- or Rc and Rd are taken together with the oxygens to form a 5 to 10 membered heterocycle;
- or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
- The compound as defined in anyone of claims 1 or 2, wherein R₂ is phenyl substituted by one or more substituent chosen from halogen, nitro, CONR₁₃R₁₄, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆ alkyloxy, C(0)C₁₋₆ alkyl, C₆₋₁₂ aryl, C₃₋₁₀ heterocycle, hydroxyl, NR₁₃R₁₄, C(0)OR₁₂, cyano, azido, wherein R₁₂, R₁₃ and R₁₄ are each independently chosen from H, C₁₋₁₂ alkyl, C₂₋₁₂ alkenyl, C₂₋₁₂ alkynyl, C₆₋₁₄ aryl, C₃₋₁₂ heterocycle, C₃₋₁₈ heteroaralkyl, C₆₋₁₈ aralkyl; or R₁₃ and R₁₄ are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
- 61. The compound as defined in anyone of claims 1 or 2, wherein R₂ is phenyl substituted by one or two substituents chosen from halogen, nitro, CONR₁₃R₁₄, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₆ alkyloxy, C(0)C₁₋₆ alkyl, C₆₋₁₂ aryl, C₃₋₁₀ heterocycle, hydroxyl, NR₁₃R₁₄, C(0)OR₁₂, cyano, azido, wherein R₁₂, R₁₃ and R₁₄ are each independently chosen from H, C₁₋₁₂ alkyl, C₂₋₁₂ alkenyl, C₂₋₁₂

alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.

- 62. The compound as defined in anyone of claims 1 or 2, wherein R₂ is phenyl substituted by one or two substituents chosen from halogen, C₁₋₆ alkyl, NR₁₃R₁₄, nitro, CONR₁₃R₁₄, C(O)OC₁₋₆ alkyl, COOH or C₁₋₆ alkyloxy C(O)OR₁₂, cyano, azido, wherein R₁₂, R₁₃ and R₁₄ are each independently chosen from H, C₁₋₁₂ alkyl, C₂₋₁₂ alkenyl, C₂₋₁₂ alkynyl, C₆₋₁₄ aryl, C₃₋₁₂ heterocycle, C₃₋₁₈ heteroaralkyl, C₆₋₁₈ aralkyl; or R₁, and R₂, are taken together with the nitrogen to form a 3
 - or R_{13} and R_{14} are taken together with the nitrogen to form a 3 to 10 membered heterocycle.
- 63. The compound as defined in anyone of claims 1 or 2, wherein R is methylphenyl.
- 64. The compound as defined in anyone of claims 1 or 2, wherein R is dichlorophenyl.
- 65. The compound as defined in anyone of claims 1 or 2, wherein R₂ is chlorophenyl.
- 66. A compound chosen from:
 - Compound 1 3-[(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-(3-IODO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
 - Compound 2 3-[(3-BENZOFURAN-2-YL-BENZYL)-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
 - Compound 3 3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
 - Compound 4 3-{(2,4-DICHLORO-BENZOYL)-[5-(3-TRIFLUOROMETHYL-PHENYL)-FURAN-2-YLMETHYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound ——	1 5	3-[(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYL)-METHYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	i 6	5-(4-FLUORO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound	1 7	3-(2,4-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	l 8	3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	1 9	3-[(2,4-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	10	5- TERT -BUTYL-3-(4-CHLORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	11	4-(TOLUENE-4-SULFONYLAMINO)-[2,3']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound	12	3-[(5-BENZOFURAN-2-YL-THIOPHEN-2-YLMETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	13	5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	14	3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-CHLORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	15	5-PHENYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound .	16	5-PHENYL-3-(TOLUENE-3-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	17 ·	3-BENZENESULFONYLAMINO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	18	3-(4-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	19	3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	20	5-TERT-BUTYL-3-(4-CHLORO-2,5-DIMETHYL- BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	21	3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	22	3-(4-METHOXY-2,3,6-TRIMETHYL-BENZENESULFONYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	23	5-PHENYL-3-(THIOPHENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	24	4-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)- [2,3']BITHIOPHENYL-5-CARBOXYLIC ACID

Compound ——	25 .	5-(3,5-BIS-TRIFLUOROMETHYL-PHENYL)-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	26	8-CHLORO-3-(4-CHLORO-2,5-DIMETHYL-BENZENESULFONYLAMINO)-4H- 1,5-DITHIA-CYCLOPENTA[A]NAPHTHALENE-2-CARBOXYLIC ACID
Compound	27	3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	28	3-[3-(2,6-DICHLORO-PYRIDIN-4-YL)-UREIDO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	29	3-(2-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	30	3-(2-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	31	5-PHENYL-3-(2-TRIFLUOROMETHOXY-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound	32	3-(4- TERT -BUTYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	33	3-(4-CHLORO-PHENOXYCARBONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	34	3-(3,4-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	35	5-PHENYL-3-(2-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound	36	3-(5-BROMO-6-CHLORO-PYRIDINE-3-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	37	3-(5-CHLORO-THIOPHENE-2-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	38	3-(5-CHLORO-3-METHYL-BENZO[B]THIOPHENE-2-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	39	3-(4-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	40	3-(3-CHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound		3-(5-CHLORO-1,3-DIMETHYL-1H-PYRAZOLE-4-SULFONYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound		3-(3-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID
Compound		3-(4-ISOPROPYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID

Compound	44	3-(2,6-DICHLORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	45	3-(2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	46	5-PHENYL-3-(5-[1,2,3]THIADIAZOL-4-YL-THIOPHENE-2- SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	47	5-PHENYL-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	48	3-(2,4-DICHLORO-BENZYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	49	3-(3-FLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	50	5-PHENYL-3-(3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound	51	3-(2-CARBOXY-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID METHYL ESTER
Compound	52	5-PHENYL-3-(4-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound	53	3-(2,5-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	54	3-(2-CYANO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	55	3-(2,5-DICHLORO-THIOPHENE-3-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	56	4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound	57	5'-CHLORO-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound	58	5-(2,4-DICHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	59	5-(4-NITRO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound .	60	3-(TOLUENE-2-SULFONYLAMINO)-5-(4-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound		5-QUINOLIN-8-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound		5-PHENYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound		5-(3-NITRO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 64	3-(TOLUENE-2-SULFÓNYLAMINO)-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 65	5-(3-CHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 66	5-(4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 67	5-(3-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 68	5-(4-CHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 69	5-(3,5-DIFLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 70	5-(3,4-DIFLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 71	3-(TOLUENE-2-SULFONYLAMINO)-5-VINYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 72	3-(4-CHLORO-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 73	3-[(4-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 74	5-PHENYL-3-[(THIOPHENE-2-CARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound 75	3-[METHYL-(THIOPHENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 76	3-(2-BROMO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 77	3-(2,4-DIFLUORO-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 78	3-[(2,4-DIFLUORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 79	3-(TOLUENE-2-SULFONYLAMINO)-5-TRIMETHYLSILANYLETHYNYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 80	5-ETHYNYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 81	3-(TOLUENE-2-SULFONYLAMINO)-5-(3-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 82	5-BENZOYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound 83	5-(4-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 84	5-(3-CHLORO-4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 85	5-(3,4-DICHLORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 86	5-PYRIDIN-4-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 87	5-PYRIDIN-3-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 88	3-(TOLUENE-2-SULFONYLAMINO)-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 89	5-(4-METHANESULFONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 90	5-(3-ACETYLAMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 91	5-(3-CHLORO-4-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 92	3-(4-METHYL-BENZOYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 93	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 94	3-(3,5-DIMETHYL-ISOXAZOLE-4-SULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 95	3-[(2-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 96 5-PHENYL-THIC	3-(2-METHYL-BENZOYLAMINO)- PHENE-2-CARBOXYLIC ACID
Compound 97	3-[METHYL-(2-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 98	5-PHENYL-3-(5-TRIFLUOROMETHYL-PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 99	5-PHENYLETHYNYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 100	3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 101	5-(2-FLUORO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 102	5-(2-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

Compound —	103	5-(2-ETHOXYCARBONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound	104	5-(2-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	105	3'-METHYL-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound	106	3-(TOLUENE-2-SULFONYLAMINO)-5-(2-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	107	3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound SULFONYL		5-STYRYL-3-(TOLUENE-2- -THIOPHENE-2-CARBOXYLIC ACID
Compound	109	3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-(4-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	110	3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound .	111	3-[[5-(3-CHLORO-4-FLUORO-PHENYL)-THIOPHEN-2-YLMETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	112	3-[(4-0XO-1-PHENYL-1,3,8-TRIAZA-SPIRO[4.5]DECANE-8-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	113	3-{[4-(2-OXO-2,3-DIHYDRO-BÈNZOIMIDAZOL-1-YL)-PIPERIDINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	114	3-{[4-(4-NITRO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	115	5-(2-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	116	5-(4-CHLORO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	117	5-(3-CYANO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	118	3-(2,5-DIMETHYL-BENZENESULFONYLAMINO)-5-P-TOLYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound	119	3-(2,4-DIFLUORO-BENZENESULFONYLAMINO)-5-P-TOLYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	120	5-PHENETHYL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	121	5-(3-ETHOXYCARBONYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID

Compound 12	2 5-(4-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 12	3 5-(3-METHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 12	4 5-(4'-BROMO-BIPHENYL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 12	5 5-(4-HYDROXYMETHYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 12	6 5-FURAN-3-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID
Compound 12	7 5-BENZOFURAN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID
Compound 12	8 5-PYRIDIN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID
Compound 12	9 5-(4-NITRO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 13	0 3-[(BENZOFURAN-2-CARBONYL)-METHYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
Compound 13	3-[(2,4-DIMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound 13	3-[[5-(2-CYANO-PHENYL)-THIOPHEN-2-YLMETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 13	5-(4-FLUORO-PHENYL)-3-(PYRIDINE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 13	5-[2-(4-CHLORO-PHENYL)-VINYL]-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 13	5 3-BENZENESULFONYLAMINO-5-(4-FLUORO-PHENYL)-THIOPHENE-2- CARBOXYLIC ACID
Compound 13	6 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 13	7 5-PHENYL-3-(2-VINYL-BENZENESULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID
Compound 13	8 3-(4-BROMO-2,5-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
Compound 13	9 3-(2-ACETYLAMINO-4-METHYL-THIAZOLE-5-SULFONYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 14	3 - (4-ACETYL-BENZENESULFONYLAMINO) - 5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID
Compound 14	1 3-(4-FLUORO-2-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 142	3-(2-METHOXY-4-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 143	3-(3,4-DIFLUORO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 144	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-5-(4-CHLORO-PHENYL)-2-METHYL-FURAN-3-CARBOXYLIC ACID ETHYL ESTER
Compound 145	3-(4-FLUORO-3-TRIFLUOROMETHYL-BENZENESULFONYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 146	3-(2-AMINO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 147	3-(3-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 148	3-(4-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 149	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 150	5-(3-CYANO-BENZYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 151	5-PHENYL-3-(2,4,6-TRIFLUORO-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 152	3-(4-METHOXY-2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 153	5-PHENYL-3-(2,3,4-TRICHLORO-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 154	5-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2-METHYL- FURAN-3-CARBOXYLIC ACID METHYL ESTER
Compound 155	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2-METHYL-1,5-DIPHENYL-1H-PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER
Compound 156	5-PHENYL-3-{[4-(3-TRIFLUOROMETHYL-PHENYL)-PIPERAZINE-1-CARBONYL]-AMIN}-THIOPHENE-2-CARBOXYLIC ACID
Compound 157	3-{[4-(4-FLUORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 158	3-{[4-(2,6-DIMETHYL-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 159	3-{[4-(2-CHLORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 160	3-{[4-(3-CHLORO-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 161	4,4'-BIS-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5,5'-DICARBOXYLIC ACID
Compound 162	3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 163	5-(1-DIMETHYLSULFAMOYL-1H-PYRAZOL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 164	5-(3-AMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 165	5-(4-AMINO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 166	5-(4-ACETYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 167	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-2,5-DIMETHYL-1H-PYRROLE-3-CARBOXYLIC ACID ETHYL ESTER
Compound 168	4-(2-CARBOXY-5-PHENYL-THIOPHEN-3-YLSULFAMOYL)-5-(4-CHLORO-PHENYL)-3-METHYL-1-PHENYL-1H-PYRROLE-2-CARBOXYLIC ACID ETHYL ESTER
Compound 169	3-(3,5-DICHLORO-4-HYDROXY-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 170	5-(1H-PYRAZOL-4-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 171	5-(3-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 172	3-[METHYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 173	3-{[2-(4-FLUORO-PHENYL)-ACETYL]-METHYL-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 174	3-(4-PENTYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 175	3-(METHYL-PHENYLACETYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 176	3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)-BENZENESULFONYLAMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 177	3-(4-METHYL-2-NITRO-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 178	5-THIAZOL-2-YL-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID
Compound 179	5-PHENYL-3-[3-(3-PHENYL-PROPYL)-UREIDO]-THIOPHENE-2-CARBOXYLIC ACID

	•
Compound 18	3-[(3,4-DIHYDRO-1H-ISOQUINOLINE-2-CARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 18	3-{[4-(4-METHOXY-PHENYL)-PIPERAZINE-1-CARBONYL]-AMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 18	2 3-{[4-(6-METHYL-PYRIDIN-2-YL)-PIPERAZINE-1-CARBONYL]- AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID HYDROCHLORIDE
Compound 18	3 3-{[4-(4-CHLORO-BENZYL)-PIPERAZINE-1-CARBONYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID HYDROCHLORIDE
Compound 18	5-(5-METHYL-PYRIDIN-2-YL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 18	5 3-[ETHYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID
Compound 18	6 3-[(3-CHLORO-THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 18	7 3-[(2-BROMO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 18	3-[(4-BUTYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID
Compound 18	9 3-(2-CHLOROMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound 19	5-(4-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 19	5-(5-CHLORO-PYRIDIN-2-YL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 19	2 5-(4-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
Compound 19	5-(4-CYANO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
Compound 19	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-NITRO-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID
Compound 19	5-(4-HYDROXYMETHYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound 19	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-NITRO-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID
Compound 19	5-(4-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
Compound 198	5-(4-METHOXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
Compound 199	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-P-TOLYL-THIOPHENE-2- CARBOXYLIC ACID

Compound 	200	5-(4-AMINO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound	201	3-[CYCLOPENTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	202.	5-BENZO[1,3]DIOXOL-5-YL-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound	203	3-[(2-HYDROXY-ETHYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	204	3-[(2,4-DICHLORO-BENZOYL)-ISOBUTYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	205	3-[(2-METHOXY-4-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	206	5-(3-CYANO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
Compound	207	5-(2-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
Compound	208	3-[(2,4-DICHLORO-BENZOYL)-PHENYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	209	3-[4-(TRIFLUOROMETHYL-BENZOYL)METHYLAMINE]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	210	3-[(4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID:
Compound	211	3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound	212	5-(3,5-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound	213	5-(3-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
Compound	214	5-(2,4-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound	215	5-(4-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
Compound	216	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-TRIFLUOROMETHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	217	5-(2-HYDROXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	218	3-[(2-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID

Compound 219	3-[(3,5-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 220	3-(4-BROMO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 221	3-(5-CARBOXY-4-CHLORO-2-FLUORO-BENZENESULFONYLAMINO)-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 222	5-PHENYL-3-(2,3,4-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 223	3-(4-BROMO-2-FLUORO-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 224	3-(4-BROMO-2-METHYL-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 225	5-(4-ISOBUTYL-PHENYL)-3-(3-METHOXY-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 226	3-[(4-FLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound 227	3-[2,5-BIS-(2,2,2-TRIFLUORO-ETHOXY)-BENZENESULFONYLAMINO]- 5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 228	3-(2-CHLORO-4-CYANO-BENZENESULFONYLAMINO)-5-(4-ISOBUTYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 229	5'-ACETYL-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound 230	5-BENZO[B]THIOPHEN-2-YL-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 231	5-(4-BUTYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 232	5-(4-ETHYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 233	3-[BENZYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound 234	3-[(4-CHLORO-2-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 235	3-[(2,4-DIMETHYL-BENZENESULFONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 236	5-(4-ACETYL-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 237	5-(4-ACETYL-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 238	5-(4-ACETYL-PHENYL)-3-(4-CHLORO-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID

Compound 239	5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID TERT-BUTYL ESTER
Compound 240	3-[(2,4-DIMETHYL-BENZENESULFONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 241	3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 242	3-ETHANESULFONYLAMINO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 243	3-[ISOPROPYL-(4-TRIFLUOROMETHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 244	3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL-BUT-2-ENYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 245	3-[(2,6-DICHLORO-PYRIDINE-3-CARBONYL)-METHYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 246	3-[(6-CHLORO-PYRIDINE-3-CARBONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 247	3-[(4-TERT-BUTYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound 248	5-(4-CARBOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 249	5-(4-ETHOXY-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE- 2-CARBOXYLIC ACID
Compound 250	3-[(2,6-DICHLORO-PYRIDINE-3-CARBONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 251	3-[(BENZO[B]THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 252	3-[METHYL-(NAPHTHALENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 253	3-[(3,4-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound 254	3-[(3,5-DICHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound 255	3-[(4-BROMO-3-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 256	3-[(3-CHLORO-BENZO[B]THIOPHENE-2-CARBONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID .
Compound 257	3-[METHYL-(4-METHYL-3-NITRO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 258	5-(4-CARBAMOYL-PHENYL)-3-(2,4-DIMETHYL- BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID

		•	•
Comp	ound 	259	5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	260	5-(1H-INDOL-5-YL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	261	3-[SEC -BUTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	262	3-[(2,4-DIMETHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	263	5-(4-AZIDO-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	264	3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	265	5-(4-CARBAMOYL-PHENYL)-3-(4-CHLORO-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	266	5-(2-FLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]- THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	267	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5- O -TOLYL-THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	268	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	269	5-(3-CHLORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Comp	ound	270	5-(3,4-DIFLUORO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compo	ound	271	5-(3-AMINO-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compo	ound	272	5-(3-ACETYL-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compo	ound	273	5-(3-HYDROXY-PHENYL)-3-[METHYL-(4-METHYL-BENZOYL)-AMINO}-THIOPHENE-2-CARBOXYLIC ACID
Compo	bund	274	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compo	ound	275	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compo	ound	276	3-[(3,4-DIMETHOXY-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compo	ound	277	3-[METHYL-(2,4,6-TRIFLUORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound	278	3-[(2,3-DIFLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	279	3-[(3-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	280	3-[(2,3-DIFLUORO-4-METHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	281	3-[(2-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	282	5-(4-CARBAMOYL-PHENYL)-3-(TOLUENE-2-SULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound	283	5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound	284	3-[(2-BROMO-4-CHLORO-BENZOYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	285	3-(2,6-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	286	3-[METHYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	287	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID METHYL ESTER
Compound	288	5-(4-CYANO-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound	289	3-(4-CHLORO-BENZENESULFONYLAMINO)-5-(4-CYANO-PHENYL)- THIOPHENE-2-CARBOXYLIC ACID
Compound	290	5-(4-CYANO-PHENYL)-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound	291	5'-ACETYL-4-(2,4-DIMETHYL-BENZENESULFONYLAMINO)- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound	292	5'-ACETYL-4-(2,6-DIMETHYL-BENZENESULFONYLAMINO)- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound	293	3-[METHYL-(4-METHYL-THIOPHENE-2-CARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	294	5-(3-CHLORO-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound	295	5'-CYANO-4-(TOLUENE-2-SULFONYLAMINO)-[2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound	296	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PYRIDIN-2-YL-THIOPHENE-2-CARBOXYLIC ACID
Compound	297	3-[(2,4-DICHLORO-THIOBENZOYL)-ISOPROPYL-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID

Compound 298	5-PHENYL-3-(2,4,6-TRIMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 299	3-[(1-CARBOXY-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 300	3-[(4-METHYL-BENZOYL)-(3-METHYL-BUT-2-ENYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 301	3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 302	3-[METHYL-(4-METHYL-BENZOYL)-AMINO]-5-PYRIDIN-3-YL-THIOPHENE-2-CARBOXYLIC ACID
Compound 303	5'-ACETYL-4-[METHYL-(4-METHYL-BENZOYL)-AMINO]- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound 304	3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-(3- TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 305	3-[ISOPROPYL-(4-METHYL-BENZOYL)-AMINO]-5-M-TOLYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound 306	3-[(2-BROMO-4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound. 307	3-[(4-CHLORO-2-FLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 308	3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-4-METHYL-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
Compound 309	3-[(2-BROMO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 310	3-[(4-CHLORO-2-IODO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 311	3-[(4-CYANO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 312	3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-[4-(2-CARBOXY-VINYL)- PHENYL]-THIOPHENE-2-CARBOXYLIC ACID
Compound 313	3-[(4-CHLORO-2-HYDROXY-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 314	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-4-METHYL-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 315	5- TERT -BUTYL-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 316	3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 317	3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 318	5-[4-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4-METHYL-BENZOYL)- PROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound 319	5-BENZOFURAN-2-YL-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)- THIOPHENE-2-CARBOXYLIC ACID
Compound 320	3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-HYDROXYMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 321	3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-METHANESULFONYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 322	5-[4-(2-CARBOXY-VINYL)-PHENYL]-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 323	3-[ALLYL-(4-METHYL-BENZOYL)-AMINO]-5-[3-(2-CARBOXY-VINYL)- PHENYL]-THIOPHENE-2-CARBOXYLIC ACID
Compound 324	3-[ISOPROPYL-(2,4,6-TRIMETHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 325	5-[3-(2-CARBOXY-ETHYL)-PHENYL]-3-[(4-METHYL-BENZOYL)-PROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound 326	3-[(2-FLUORO-4-TRIFLUOROMETHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 327	3-[TERT -BUTYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 328	3-[(2-AMINO-4-CHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 329	3-[(4-CHLORO-2-NITRO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 330	3-[(4-METHYL-BENZOYL)-(3-TRIFLUOROMETHYL-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 331	3-[(3-FLUORO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 332	5-(4-CARBOXY-PHENYL)-3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound 333	3-[CYCLOPROPYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 334	3-[(3-TERT-BUTYL-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 335	3-[(3-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 336	3-[(2,4-DIFLUORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 337	3-[(4-CHLORO-2,5-DIFLUORO-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 338	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(2-METHYL-ALLYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 339	3-{ALLYL-[2-(4-CHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 340	3-[BENZYL-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 341	3-[(4-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 342	3-[(4-METHYL-BENZOYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
Compound 343	3-[(4-METHYL-BENZOYL)-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 344	3-[(3-METHOXY-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 345	3-[(2-CHLORO-BENZYL)-(4-METHYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 346	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-ISOBUTYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 347	3-[ALLYL-(2-NAPHTHALEN-2-YL-ACETYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
Compound 348	3-{ALLYL-[2-(2,4-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 349	3-{ALLYL-[2-(2-CHLORO-4-FLUORO-PHENYL)-ACETYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 350	3-{ALLYL-[2-(3,4-DICHLORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 351	3-{ALLYL-[2-(2,4-DIFLUORO-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 352	3-{ALLYL-[2-(4-TRIFLUOROMETHYL-PHENYL)-ACETYL]-AMINO}-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 353	3-{ALLYL-[2-(2,6-DICHLORO-PHENYL)-ACETYL}-AMINO}-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
Compound 354	3-[ALLYL-(2-M-TOLYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 355	5-(4-ACETYL-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID

Compound	356	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-FLUORO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	357	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-M-TOLYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	358	5'-ACETYL-4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound .	359	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	360	4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5'-METHYL- [2,2']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound .	361	3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-(4-METHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	362	3-(CYCLOHEXANECARBONYL-ISOPROPYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	363	3-{(2,4-DICHLORO-BENZOYL)-[1-(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	364	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYL-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT -BUTYL ESTER
Compound	365	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT -BUTYL ESTER
Compound	366	3-[(4-METHYL-BENZOYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	367	5'-ACETYL-4-(2,4-DIMETHYL-BENZENESULFONYLAMINO)- [2,3']BITHIOPHENYL-5-CARBOXYLIC ACID
Compound	368	3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	369	5-(4-METHANESULFONYLAMINO-PHENYL)-3-(TOLUENE-2- SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound		3-(4-FLUORO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
Compound	371	3-[(3-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	372	3-(4-CHLORO-2-METHYL-BENZENESULFONYLAMINO)-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID
Compound	373	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4- METHANESULFONYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	374	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(4-METHANESULFINYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID

Compound 375	5-(4-CARBOXY-PHENYL)-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound 376	5-BENZOFURAN-2-YL-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound 377	3-[(2-ACETOXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 378	3-[ISOPROPYL-(2-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 379	3-[ISOPROPYL-(2-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 380	3-(CYCLOHEPTANECARBONYL-ISOPROPYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 381	3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 382	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-METHYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 383	3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(3-NITRO-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 384	3-[(3-CYCLOPENTYL-PROPIONYL)-METHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 385	3-(BUTYRYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC
Compound 386	3-(METHYL-PENT-4-ENOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 387	3-[ISOPROPYL-(5-METHYL-3-OXO-3H-ISOINDOL-1-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 388	3-[METHYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 389	3-(METHYL-PENTANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 390	3-[METHYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 391	3-(CYCLOPENTANECARBONYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 392	3-[(3-CYCLOPENTYL-PROPIONYL)-ETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 393	3-(CYCLOBUTANECARBONYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 394	3-(BUT-2-ENOYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound	395	3-[ISOPROPYL-(4-METHYL-2-VINYL-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	396	3-[ISOPROPYL-(4-METHYL-CYCLOHEX-1-ENECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	397	3-(ALLYL-HEXANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	398 ·	3-(ALLYL-CYCLOBUTANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	399	3-(ALLYL-PENTANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	400	3-[ALLYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	401	3-[ALLYL-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	402	3-[(2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	403	3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	404	3-[(2,4-DICHLORO-BENZOYL)-(1-PHENYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	405	3-[ISOPROPYL-(3-METHYL-CYCLOPENT-3-ENECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	406	3-[(2-BENZYLOXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	407	3-[(2,4-DIMETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	408	3-[ISOPROPYL-(3-METHYL-CYCLOPENTANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	409	3-[(2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	410	5-PHENYL-3-[PROPIONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound	411	3-[ISOBUTYRYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	412	3-[(3-METHYL-BUTYRYL)-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	413	3-[CYCLOPROPANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	414	3-[CYCLOBUTANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound — _	415	3-[BUTYRYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	416	3-[(2-CYCLOPENTYL-ACETYL)-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	417	3-[(4-TERT-BUTYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	418	3-[(4-NITRO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	419	3-[(3-METHYL-BUTYRYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	420	3-[CYCLOPROPANECARBONYL-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	421	3-[(2-CHLORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	422	3-[(2-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	423	3-[(2-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	424	3-[(ADAMANTANE-1-CARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	425	3-[(2-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	426	3-[ACETYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	427	3-[(2-METHYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	428	3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-(3-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	429	3-[(1-ACETYL-PIPERIDIN-4-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	430	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-[4-(1 H - TETRAZOL-5-YL)-PHENYL]-THIOPHENE-2-CARBOXYLIC ACID
Compound	431	3-[(2-CYANO-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	432 -	3-[CYCLOBUTANECARBONYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	433	3-[BUTYRYL-(2-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

•	
Compound 434	3-[ACETYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 435	3-[CYCLOBUTANECARBONYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 436	3-[CYCLOHEXANECARBONYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 437	3-[(4-TERT-BUTYL-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 438	3-[(4-TERT-BUTYL-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 439	3-[(4-TERT-BUTYL-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 440	3-[(4-TERT-BUTYL-BENZYL)-BUTYRYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 441	3-[(4-TERT-BUTYL-BENZYL)-CYCLOHEXANECARBONYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 442	3-[(4-TERT-BUTYL-BENZYL)-(2-CYCLOPENTYL-ACETYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 443	3-[(2-CYCLOPENTYL-ACETYL)-(4-NITRO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 444	3-[(2-CHLORO-BENZYL)-CYCLOHEXANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 445	3-[(2-CYCLOPENTYL-ACETYL)-(3-METHYL-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 446	3-[BUTYRYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 447	3-[BUTYRYL-(2-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 448	3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5- M - TOLYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 449	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-THIAZOL-2-YL-THIOPHENE-2-CARBOXYLIC ACID
Compound 450	3-(ACETYL-BENZYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 451	3-(BENZYL-PROPIONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 452	3-[BENZYL-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 453	3-[BENZYL-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

	Compound 	454	3-(BENZYL-CYCLOPROPANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	455	3-[ACETYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	456	3-[(4-CHLORO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	457	3-[(4-CHLORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
	Compound	458	3-[(4-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	459	3-[(4-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	460	5-(4-ACETYL-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
	Compound	461	3-[(4-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	462	3-[BUTYRYL-(4-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	463	3-[(4-CHLORO-BENZYL)-(2-CYCLOPENTYL-ACETYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
•	Compound	464	3-[ACETYL-(4-TRIFLUOROMETHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	465	3-[ISOBUTYRYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
	Compound	466	3-[CYCLOPROPANECARBONYL-(3-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	467	3-[(4-METHYL-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	468	3-[ISOBUTYRYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
	Compound	469	3-[CYCLOPROPANECARBONYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	470	3-[BUTYRYL-(4-METHYL-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
	Compound	471	3-[(3-METHOXY-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
	Compound	472	3-[(3-METHOXY-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID

Compound	473	·3-[CYCLOBUTANECARBONYL-(3-METHOXY-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	474	3-[(2-CARBAMOYL-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	475	3-[BUTYRYL-(3-METHOXY-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	476	3-[ACETYL-(3-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	477	3-[(3-CHLORO-BENZYL)-PROPIONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	478	3-[(3-CHLORO-BENZYL)-(2-METHOXY-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	479	3-[(3-CHLORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	480	3-[(3-CHLORO-BENZYL)-CYCLOPROPANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	481	3-[(3-CHLORO-BENZYL)-CYCLOBUTANECARBONYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	482	3-[BUTYRYL-(3-CHLORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	483	3-[ACETYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound	484	3-[(2,4-DIFLUORO-BENZYL)-(2-METHOXY-ACETYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	485	3-[(2,4-DIFLUORO-BENZYL)-ISOBUTYRYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	486	3-[(2,4-DIFLUORO-BENZYL)-(3-METHYL-BUTYRYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	487	3-[BENZYL-(2-CYCLOPENTYL-ACETYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	488	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-(1H-INDOL-5-YL)-THIOPHENE-2-CARBOXYLIC ACID
Compound	489	3-(BENZYL-CYCLOBUTANECARBONYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	490	3-[CYCLOHEXANECARBONYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	491	3-{ALLYL-[2-(4-METHOXY-PHENYL)-ACETYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	492	3-(ETHYL-HEXANOYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound 493	3-(BUTYRYL-ETHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 494	3-[ETHYL-(4-METHYL-PENTANOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 495	3-[CYCLOBUTANECARBONYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 496	3-[BUTYRYL-(2,4-DIFLUORO-BENZYL)-AMINO]-5-PHENYL-THIOPHENE- 2-CARBOXYLIC ACID
Compound 497	3-(CYCLOPENTANECARBONYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 498	3-(CYCLOHEXANECARBONYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 499	3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PYRROLIDINE-1-CARBOXYLIC ACID TERT-BUTYL ESTER
Compound 500	3-[(1,4-DIMETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 501	5-(4-ETHYL-PHENYL)-3-[(2-HYDROXY-4-METHYL-BENZOYL)- ISOPROPYL-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound 502	3-[(2-HYDROXY-4-METHYL-BENZOYL)-ISOPROPYL-AMINO]-5- M - TOLYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 503	3-[(2,4-DICHLORO-BENZOYL)-PYRROLIDIN-3-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 504	4-{5-CARBOXY-4-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO-2H-PYRIDINE-1-CARBOXYLIC ACID BENZYL ESTER
Compound 505	3-{[2-(HYDROXYIMINO-METHYL)-4-METHYL-BENZOYL}-ISOPROPYL-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 506	3-[(1-CARBAMIMIDOYL-PIPERIDIN-4-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 507	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-AZEPANE-1-CARBOXYLIC ACID TERT -BUTYL ESTER
Compound 508	4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER
Compound 509	3-[AZEPAN-4-YL-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 510	3-[(4-METHYL-CYCLOHEXANECARBONYL)-PIPERIDIN-4-YL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID LITHIUM SALT

Compound 511	3-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PIPERIDINE-1-CARBOXYLIC ACID TERT -BUTYL ESTER
Compound 512	3-[(4-BENZYLOXYCARBONYLAMINO-CYCLOHEXYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 513	3-[ISOPROPYL-(4-METHYL-2-OXO-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 514	3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-3-YL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH GENERIC INORGANIC NEUTRAL COMPONENT
Compound 515	3-[(4-BENZYLOXYCARBONYLAMINO-CYCLOHEXYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 516	3-[(2-BENZYLOXY-1-METHYL-ETHYL)-(2,4-DICHLORO-BENZOYL)- AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 517	3-[(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 518	3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-1-HYDROXYMETHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 519	3-[(2,4-DICHLORO-BENZOYL)-PIPERIDIN-4-YLMETHYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 520	3-[(2-CHLORO-BENZOYL)-PIPERIDIN-4-YLMETHYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 521	3-[(4,6-DICHLORO-1H-INDOLE-2-CARBONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 522	3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-1-METHYL-ETHYL)- AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 523	4-{1-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-ETHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER
Compound 524	4-{5-CARBOXY-4-{ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHEN-2-YL}-3,6-DIHYDRO-2 H -PYRIDINE-1-CARBOXYLIC ACID BENZYL ESTER
Compound 525	3-[(4-METHYL-CYCLOHEXANECARBONYL)-PYRIDIN-4-YL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 526	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-5-PIPERIDIN-4-YL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID
Compound 527	3-[ISOPROPYL-(4-PROPYL-CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 528	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-CYCLOHEXYL-AMMONIUM; TRIFLUORO-ACETATE

Compound 529 —_	3-[(2,4-DICHLORO-BENZOYL)-(1-PIPERIDIN-4-YL-ETHYL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID
Compound 530	3-[(CYCLOHEX-3-ENECARBONYL)-ISOPROPYL-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 531	3-[(4-ETHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 532	3-[(4-CHLORO-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 533	4-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-3-METHYL-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER
Compound 534	3-[(2,4-DICHLORO-BENZOYL)-(2-METHOXY-CYCLOHEXYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 535	3-[(2,4-DICHLORO-BENZOYL)-(2,2-DIMETHYL-[1,3]DIOXAN-5-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 536	3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(1-METHYL-PIPERIDIN-4-YL)-THIOPHENE-2-CARBOXYLIC ACID
Compound 537	3-[(2,4-DICHLORO-BENZOYL)-(3-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID; COMPOUND WITH TRIFLUORO-ACETIC ACID
Compound 538	3-[(2,4-DICHLORO-BENZOYL)-(2-HYDROXY-CYCLOHEXYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 539	'4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYLCYCLOHEXANE CARBONYL)-AMINO]-METHYL}-PIPERIDINE-1-CARBOXYLIC ACID BENZYL ESTER
Compound 540	3-[((1R,2s,4r)-2-HYDROXY-4-METHYL-CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 541	3-{ISOPROPYL-[1-(4-METHOXY-2,3,6-TRIMETHYL-BENZENESULFONYL)-5-METHYL-1,2,3,6-TETRAHYDRO-PYRIDINE-2-CARBONYL]-AMINO}-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 542	3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]-4-FLUORO-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 543	3-[(2,4-DICHLORO-BENZOYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound 544	4-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(4-METHYLCYCLOHEXANE CARBONYL)-AMINO]-METHYL}-PIPERIDINIUM; TRIFLUORO-ACETATE
Compound 545	3-[(2-TERT-BUTOXYCARBONYLAMINO-1-METHYL-ETHYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID

Compound	546	2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-PROPYL-AMINE TRIFLUOROACETIC ACID SALT
Compound	547	3-[(3-CARBOXY-CYCLOPENTYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	548	3-[(3-CARBOXY-CYCLOPENTYL)-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	54	9 2-[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-
Compound	550	BENZOYL)-AMINO]-CYCLOHEXYL-AMMONIUM CHLORIDE 3-(BENZOYL-METHYL-AMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound		551 {[5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2-CARBONYL]-AMINO)-ACETIC ACID
Compound		552 5-BROMO-3-(TOLUENE-2-SULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID
Compound		553 3-[CYCLOHEXYL-(2,4-DICHLORO-BENZOYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound		3-[[1,3]DIOXAN-5-YL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound	555	3-[[2-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-1-METHYL-2-PHENYL-ETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound		556 3-[[2-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-1-METHYL-2-PHENYL-ETHYL]-(2,4-DICHLORO-BENZOYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound		557 3-[(2,4-DICHLORO-BENZOYL)-(2-DIETHYLAMINO-THIAZOL- 5-YLMETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound		558 (5-{[(2-CARBOXY-5-PHENYL-THIOPHEN-3-YL)-(2,4-DICHLORO-BENZOYL)-AMINO]-METHYL}-THIAZOL-2-YL)-DIETHYL-AMMONIUM; CHLORIDE
Compound		559 5-(4-FLUORO-PHENYL)-3-[ISOPROPYL-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID
Compound		560 3-['((1S,2R,4S)-2-HYDROXY-4-METHYL- CYCLOHEXANECARBONYL)-ISOPROPYL-AMINO]-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID
Compound	561	3-[(2,4-DICHLORO-BENZOYL)-(2-METHOXY-1-METHYL-ETHYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound		562 3-[(4S)-ISOPROPYL-(4-METHYL-CYCLOHEX-1- ENECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID
Compound		566 3-METHYL-(4-METHYLBENZOYL)-AMINO)5-PHENYL THIOPHENE-2-CARBOXYLIC ACID (2-HYDROXY-ETHYL)AMIDE
Compound		567 5-PHENYL-3-(TOLUENE-4-SULFONYLAMINO)-THIOPHENE-2- CARBOXYLIC ACID CYCLOBUTYLAMIDE

Compound —	568 3-(2,4-DIMETHYL-BENZENESULFONYLAMINO)-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID AMIDE	
Compound	569 5-BROMO-3-[(2,4-DICHLORO-BENZOYL)-ISOPROPYL-AMINO]- THIOPHENE-2-CARBOXYLIC ACID	
Compound	570 5-(4-CHLORO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANE-CARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	
Compound	571 5-(4'-CHLORO-BIPHENYL-4-YL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	
Compound	572 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(TETRAHYDRO- PYRAN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
Compound	573 3-[(4-METHYL-CYCLOHEXANECARBONYL)-(1-METHYL-PIPERIDIN-4-YL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
Compound	574 3-[(4-METHYL-CYCLOHEXANECARBONYL)-PIPERIDIN-4-YL-AMINO]- 5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
Compound	575 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(4-TRIFLUOROMETHYL-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	
Compound	576 5-(4-CYANO-PHENYL)-3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-THIOPHENE-2-CARBOXYLIC ACID	
Compound	577 3-[ISOPROPYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5-(4-METHOXY-PHENYL)-THIOPHENE-2-CARBOXYLIC ACID	
Compound ,	578 3-[(2-METHOXY-1-METHYL-ETHYL)-(4-METHYL- CYCLOHEXANECARBONYL)-AMINO]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
Compound	579 3-[CYCLOHEXYL-(4-METHYL-CYCLOHEXANECARBONYL)-AMINO]-5- PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
Compound	581 5-(4-ISOBUTYL-PHENYL)-3-[5-(5-TRIFLUOROMETHYL-ISOXAZOL-3-YL)-THIOPHENE-2-SULFONYLAMINO]-THIOPHENE-2-CARBOXYLIC ACID	
Compound	5825-(4-ISOBUTYL-PHENYL)-3-(2,3,4-TRIFLUORO-BENZENESULFONYLAMINO)-THIOPHENE-2-CARBOXYLIC ACID	
Compound	583 3-[(2,4-DICHLORO-PHENYL)-ISOPROPYL-CARBAMOYL]-5-PHENYL-THIOPHENE-2-CARBOXYLIC ACID	
Compound	584 3- (METHYL-P-TOLYL-CARBAMOYL)-5-PHENYL-THIOPHENE-2- CARBOXYLIC ACID	
Compound	585 3-[(2,4-DICHLORO-PHENYL)-METHYL-CARBAMOYL]-5-PHENYL- THIOPHENE-2-CARBOXYLIC ACID	
or pharmaceutically acceptable salts thereof.		

67. A method for treating or preventing a Flaviviridae viral infection in a host comprising administering to the host a therapeutically effective amount of at least one compound having the formula III:

or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N$$
 R_2
or
 N
 R_3
 R_3

wherein,

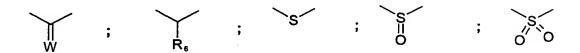
M is chosen from:

wherein,

 R_4 is chosen from H or C $_{1-6}$ alkyl;

 $\rm R_8$ is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and $\rm R_{15}$ is chosen from H or C $_{1-6}$ alkyl;

J is chosen from:



wherein,

W is chosen from O, S or NR,,

wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-12}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-12}$ aralkyl;

and R_{ϵ} is chosen from H, C $_{1-12}$ alkyl, C $_{6-12}$ aryl or C $_{6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{a}OR_{b}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$ tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{9})-SO_{2}-R_{5}$, $CONR_{9}OH$ or halogen, wherein R_{9} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl; or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1\text{-}12}$ alkyl, C $_{2\text{-}12}$ alkenyl, C $_{2\text{-}12}$ alkynyl, C $_{6\text{-}14}$ aryl, C $_{3\text{-}12}$ heterocycle, C $_{3\text{-}18}$ heteroaralkyl and C $_{6\text{-}18}$ aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

 R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl, or halogen;

 R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl. C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

 R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

.Z is chosen from H, halogen, C, alkyl.

- 68. The method of claim 65, further comprising at least one antiviral agent.
- 69. The method according to claim 66, wherein the antiviral agent is chosen from a viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor.
- 70. The method according to claim 66, wherein the antiviral agent is chosen from interferon α and ribavirin.
- 71. The method according to anyone of claims 66 to 68, wherein said compound and said antiviral agent are administered sequentially.
- 72. The method according to anyone of claims 66 to 68, wherein said compound and said antiviral agent are administered simultaneously.
- 73. The method of claim 65, further comprising at least one additional agent chosen from immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.
- 74. The method of claim 71, wherein said additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.

75. The method according to anyone of claims 71 or 72, wherein said_compound and said additionnal agent are administered sequentially.

- 76. A method according to anyone of claims 71 or 72, wherein said compound and said additionnal agent are administered simultaneously.
- 77. The method as defined in anyone of claims 65 to 74, wherein said Flaviviridea viral infection is hepatitis C viral infection (HCV).
- 78. A pharmaceutical composition comprising at least one compound having the formula III:

or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N$$
 R_2 or R_3
 R_3

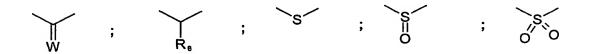
wherein, M is chosen from:

wherein,

R4 is chosen from H or C 1-6 alkyl;

 $\rm R_8$ is chosen from H, C $_{1\text{-}12}$ alkyl, C $_{2\text{-}12}$ alkenyl, C $_{2\text{-}12}$ alkynyl, C $_{6\text{-}14}$ aryl, C $_{3\text{-}12}$ heterocycle, C $_{3\text{-}12}$ heteroaralkyl, C $_{6\text{-}16}$ aralkyl; and $\rm R_{15}$ is chosen from H or C $_{1\text{-}6}$ alkyl;

J is chosen from:



wherein W is chosen from O, S or NR,

wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{12}$ alkynyl, C $_{6-12}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl;

and R_{ϵ} is chosen from H, C $_{1-12}$ alkyl, C $_{6-12}$ aryl or C $_{6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{6}OR_{5}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently

chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl, C $_{6-18}$ aralkyl; or R $_{10}$ and R $_{11}$ are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl and C $_{6-18}$ aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

 R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-16} heteroaralkyl, C_{6-18} aralkyl or halogen;

R₂ is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

 R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

Z is chosen from H, halogen, C, alkyl; and

at least one pharmaceutically acceptable carrier or excipient.

- 79. A pharmaceutical composition as defined in claim 76, further comprising one or more additional agent is chosen from antiviral agent, immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.
- 80. The pharmaceutical composition as defined in claim 77, wherein the antiviral agent is chosen from a viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor.

81. The pharmaceutical composition as defined in claim 77, wherein the antiviral agent is chosen from interferon α and ribavirin.

- 82. The pharmaceutical composition as defined in claim 77, wherein said additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.
- 83. The composition as defined in anyone of claims 76-80 wherein said Flaviviridae viral infection is hepatitis C viral infection (HCV).
- 84. The use of a compound having the formula III:

or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N$$
 R_2 or R_2 ;

wherein, M is chosen from:

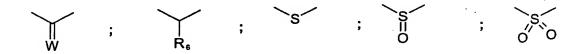
$$R_{4}$$
 , R_{15} , R_{15} , R_{15} , R_{8} , a bond ,

wherein,

 R_4 is chosen from H or C $_{1-6}$ alkyl;

 $\rm R_8$ is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-16}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and $\rm R_{15}$ is chosen from H or C $_{1-6}$ alkyl;

J is chosen from:



wherein W is chosen from O, S or NR,,

wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-12}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R $_6$ is chosen from H, C $_{1-12}$ alkyl, C $_{6-12}$ aryl or C $_{6-16}$ aralkyl;

Y is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{2}OR_{5}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently

chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl, C $_{6-18}$ aralkyl; or R $_{10}$ and R $_{11}$ are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

- R_a and R_b are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl and C $_{6-18}$ aralkyl;
- or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;
- R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;
- R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl or halogen;
- R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;
- R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-16} heteroaralkyl or C_{6-16} aralkyl;
- Z is chosen from H, halogen, C₁₋₆ alkyl;

for the manufacture of a medicament for treating or preventing a viral Flaviridea infection in a host.

- 85. The use as defined in claim 84, wherein said Flaviviridae viral infection is hepatitis C viral infection (HCV).
- 86. The use of a compound having the formula III:

or pharmaceutically acceptable salts thereof in therapy;

wherein,

X is chosen from:

$$N_{R_3}^{M}$$
 or $N_{R_3}^{R_2}$;

wherein,

M is chosen from:

$$R_4$$
, R_{15}

wherein,

R₄ is chosen from H or C ₁₋₆ alkyl;

 $R_{\rm g}$ is chosen from H, C $_{\rm 1-12}$ alkyl, C $_{\rm 2-12}$ alkenyl, C $_{\rm 2-12}$ alkynyl, C $_{\rm 6-14}$ aryl, C $_{\rm 3-12}$ heterocycle, C $_{\rm 3-12}$ heteroaralkyl, C $_{\rm 6-16}$ aralkyl; and $R_{\rm 15}$ is chosen from H or C $_{\rm 1-6}$ alkyl;

J is chosen from:

$$\bigvee_{W} \stackrel{--}{;} \qquad \bigvee_{R_e} \qquad ; \qquad \stackrel{\backslash S}{:} \qquad ;$$

wherein W is chosen from O, S or NR,

wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkenyl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R $_6$ is chosen from H, C $_{1-12}$ alkyl, C $_{6-12}$ aryl or C $_{6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{a}OR_{b}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl; or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 $\rm R_a$ and $\rm R_b$ are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl and C $_{6-18}$ aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

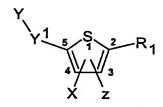
 R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl or halogen;

 R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

R₃ is chosen from H, C₁₋₁₂ alkyl, C₂₋₁₂ alkenyl, C₂₋₁₂ alkynyl, C₆₋₁₄ aryl. C₃₋₁₂ heterocycle, C₃₋₁₈ heteroaralkyl or C₆₋₁₈ aralkyl;

Z is chosen from H, halogen, C1-6 alkyl.

87. The use of a compound having the formula III:



(III) or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N$$
 R_2 or N
 R_3
 R_3

wherein,

M is chosen from:

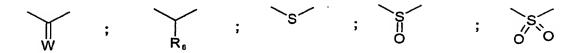
$$R_4$$
 wherein,

R₄ is chosen from H or C ₁₋₆ alkyl;

 R_8 is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and

 R_{15} is chosen from H or C $_{1-6}$ alkyl;

J is chosen from:



wherein W is chosen from O, S or NR,

wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-12}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R $_{6}$ is chosen from H, C $_{1-12}$ alkyl, C $_{6-12}$ aryl or C $_{6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{2}OR_{5}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{9})-SO_{2}-R_{5}$, $CONR_{9}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl; or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-16}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

 R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl, or halogen;

 R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

 R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

Z is chosen from H, halogen, C1-6 alkyl;

for treating or preventing Flaviviridae viral infection in a host.

- 88. The use of a compound as defined in claim 85, further comprising one or more additional agent chosen from antiviral agent, immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.
- 89. The use as defined in claim 86, wherein said antiviral agent is chosen from a viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor.
- 90. The use as defined in claim 86, wherein said antiviral agent is chosen from interferon α and ribavirin.
- 91. The use of as defined in claim 86 wherein said additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine or cyclosporin.
- 92. The use as defined in anyone of claims 86 to 89, wherein said compound and said additionnal agent are administered sequentially.

93. The use as defined in anyone of claims 86 to 89, wherein said compound and said additionnal agent are administered simultaneously.

- 94. The use as defined in anyone of claims 85 to 91, wherein said Flaviviridea viral infection is hepatitis C viral infection (HCV).
- 95. A method for inhibiting or reducing the activity of viral polymerase in a host comprising administering a therapeutically effective amount of a compound having the formula III:

or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N \stackrel{M}{\sim} R_2$$
 or $N \stackrel{R_2}{\sim} R_3$;

wherein,

M is chosen from:

wherein,

R₄ is chosen from H or C 1-6 alkyl;

 $\rm R_8$ is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and $\rm R_{15}$ is chosen from H or C $_{1-6}$ alkyl;

J is chosen from:

wherein W is chosen from O, S or NR,,

wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkenyl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R $_6$ is chosen from H, C $_{1-12}$ alkyl, C $_{6-16}$ aryl or C $_{6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{a}OR_{b}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

- R_a and R_b are each independently chosen from H, C $_{1\text{--}12}$ alkyl, C $_{2\text{--}}$ alkenyl, C $_{2\text{--}12}$ alkynyl, C $_{6\text{--}14}$ aryl, C $_{3\text{--}12}$ heterocycle, C $_{3\text{--}18}$ heteroaralkyl and C $_{6\text{--}18}$ aralkyl;
- or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;
- R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;
- R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl, or halogen;
- R_{z} is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-19} aralkyl;
- R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;
- Z is chosen from H, halogen, C1-6 alkyl.
- 96. The method as defined in claim 93, further comprising one or more viral polymerase inhibitor.
- 97. The method as defined in anyone of claims 93 or 94, wherein said viral polymerase is a Flaviviridae viral polymerase.
- 98. The method as defined in anyone of claims 93 or 94, wherein said viral polymerase is a RNA-dependant RNA-polymerase.
- 99. The method as defined in anyone of claims 93 or 94, wherein said viral polymerase is HCV polymerase.

100. A method for inhibiting or reducing the activity of viral helicase in a host comprising administering a therapeutically effective amount of a compound having the formula III:

or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N_{R_3}^{M}$$
 or $N_{R_3}^{R_2}$;

wherein,

M is chosen from:

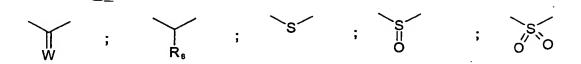
$$R_4$$
, R_{15}

wherein,

R4 is chosen from H or C 1-6 alkyl;

 R_8 is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R_{15} is chosen from H or C $_{1-6}$ alkyl;

J is chosen from:



wherein W is chosen from O, S or NR,

wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-12}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R $_{6}$ is chosen from H, C $_{1-12}$ alkyl, C $_{6-12}$ aryl or C $_{6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{8}OR_{b}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl; or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl and C $_{6-18}$ aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

 R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl or halogen;

 R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

 R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

- Z is chosen from H, halogen, C, alkyl.
- 101. The method as defined in claim 98, wherein said compound is chosen from:
 - Compound #14 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-chloro-phenyl)-thiophene-2-carboxylic acid
 - Compound #19 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid
 - Compound #223 3-(4-Bromo-2-fluorobenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid
 - Compound #224 3-(4-Bromo-2-methylbenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid
 - Compound #225 5-(4-Isobutylphenyl 3-(3-methoxy-benzenesulfonyl-amino)-thiophene-2-carboxylic acid
 - Compound #581 5-(4-Isobutyl-phenyl)-3-[5-(5-trifluoromethyl-isoxazol-3-yl)-thiophene-2-sulfonylamino]thiophene-2-carboxylic acid
 - Compound #227 3-[2,5-Bis-(2,2,2-trifluoroethoxy)
 benzenesulfonylamino]-5-(4-isobutyl-phenyl)
 thiophene-2-carboxylic acid
 - Compound #228 3-(2-Chloro-4-cyanobenzenesulfonylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid
 - Compound #582 5-(4-Isobutyl-phenyl)-3-(2,3,4-trifluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid or pharmaceutically acceptable salts thereof.
- 102. The method as defined in anyone of claims 98 or 99, wherein said viral helicase is a flaviviridea helicase
- 103. The method as defined in anyone of claims 98 or 99, wherein said viral helicase is HCV helicase.

104. The use of a compound having the formula III:

or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N$$
 R_2
or
 N
 R_3

wherein,

M is chosen from:

$$R_4$$
; R_{15}

wherein,

 R_4 is chosen from H or C $_{1-6}$ alkyl;

 $\rm R_8$ is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and $\rm R_{15}$ is chosen from H or C $_{1-6}$ alkyl;

J is chosen from:

wherein W is chosen from O, S or NR, wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-12}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R $_{6}$ is chosen from H, C $_{1-12}$ alkyl, C $_{6-12}$ aryl or C $_{6-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{5}OR_{5}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl; or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl and C $_{6-18}$ aralkyl;

or $R_{\rm b}$ and $R_{\rm b}$ are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-16}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

 R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl or halogen;

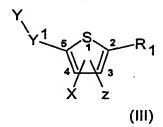
 R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

 R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

Z is chosen from H, halogen, C1-6 alkyl;

for inhibiting or reducing the activity of viral polymerase in a host.

- 105. The use as defined in claim 102 further comprising one or more viral polymerase inhibitor.
- 106. The use as defined in anyone of claims 102 or 103, wherein said viral polymerase is Flaviviridae viral polymerase.
- 107. The use as defined in anyone of claims 102 or 103 wherein said viral polymerase is RNA-dependent RNA-polymerase.
- 108. The use as defined in anyone of claims 102 or 103, wherein said viral polymerase is HCV polymerase.
- 109. The use of a compound having the formula III:



or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N$$
 R_2
or
 N
 R_3

wherein,

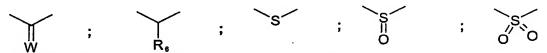
M is chosen from:

wherein,

 R_4 is chosen from H or C $_{1-6}$ alkyl;

 R_8 is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R_{15} is chosen from H or C $_{1-6}$ alkyl;

J is chosen from:



wherein W is chosen from O, S or NR,,

wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-12}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl;

and R_{ϵ} is chosen from H, C $_{1-12}$ alkyl, C $_{\epsilon-12}$ aryl or C $_{\epsilon-16}$ aralkyl;

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{5}OR_{5}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{9})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{9})-SO_{2}-R_{5}$, $CONR_{9}OH$ or halogen, wherein R_{9} , R_{5} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl;

or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1\text{-}12}$ alkyl, C $_{2\text{-}12}$ alkenyl, C $_{2\text{-}12}$ alkynyl, C $_{6\text{-}14}$ aryl, C $_{3\text{-}12}$ heterocycle, C $_{3\text{-}18}$ heteroaralkyl and C $_{6\text{-}18}$ aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

 R_{1} is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl or halogen;

 R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

 R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

Z is chosen from H, halogen, C1-6 alkyl;

for inhibiting or reducing the activity of viral helicase in a host.

- 110. The use as defined in claim 109, wherein said compound is chosen from:
 - Compound #14 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-chloro-phenyl)-thiophene-2-carboxylic acid
 - Compound #19 3-(4-Chloro-2,5-dimethyl-benzenesulfonylamino)-5-(4-isobutyl-phenyl)-thiophene-2-carboxylic acid
 - Compound #223 3-(4-Bromo-2-fluorobenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid
 - Compound #224 3-(4-Bromo-2-methylbenzenesulfo-nylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid
 - Compound #225 5-(4-Isobutylphenyl 3-(3-methoxy-benzenesulfonyl-

amino)-thiophene-2-carboxylic acid

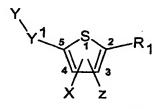
Compound #581 5-(4-Isobutyl-phenyl)-3-[5-(5-trifluoromethyl-isoxazol-3-yl)-thiophene-2-sulfonylamino]-thiophene-2-carboxylic acid

Compound #227 3-[2,5-Bis-(2,2,2-trifluoroethoxy)
benzenesulfonylamino]-5-(4-isobutyl-phenyl)thiophene-2-carboxylic acid

Compound #228 3-(2-Chloro-4-cyanobenzenesulfonylamino)-5-(4-isobutylphenyl)-thiophene-2-carboxylic acid

Compound #582 5-(4-Isobutyl-phenyl)-3-(2,3,4-trifluoro-benzenesulfonylamino)-thiophene-2-carboxylic acid or pharmaceutically acceptable salts thereof.

- 111. The use as defined in anyone of claims 109 and 110 further comprising one or more viral helicase inhibitor.
- 112. The use as defined in anyone of claims 109 or 111, wherein said viral helicase is Flaviviridae viral helicase.
- 113. The use as defined in anyone of claims 109 or 111, wherein said viral helicase is HCV helicase.
- 114. A combination comprising a compound having the formula III:



(III)

or pharmaceutically acceptable salts thereof;

wherein,

X is chosen from:

$$N$$
 R_2 or R_3
 R_3

wherein, M is chosen from:

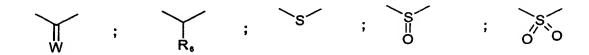
$$R_4$$
, R_{15}

wherein,

 $\rm R_4$ is chosen from H or C $_{1-6}$ alkyl; $\rm R_8$ is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and

J is chosen from:

R₁₅ is chosen from H or C ₁₋₆ alkyl;



wherein W is chosen from O, S or NR, wherein R, is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-12}$ aryl, C $_{3-12}$ heterocycle, C $_{3-12}$ heteroaralkyl, C $_{6-16}$ aralkyl; and R $_{6}$ is chosen from H, C $_{1-12}$ alkyl, C $_{6-12}$ aryl or C $_{6-16}$

 Y^1 is chosen from a bond, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{2}OR_{5}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$ or halogen, wherein R_{5} , R_{5} , R_{10} and R_{11} are each independently

chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-16}$ heteroaralkyl, C $_{6-16}$ aralkyl; or R $_{10}$ and R $_{11}$ are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 R_a and R_b are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl and C $_{6-18}$ aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

 R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl, or halogen;

 R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

 R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

Z is chosen from H, halogen, C, alkyl;

and one or more additionnal agent chosen from viral serine protease inhibitor, viral polymerase inhibitor and viral helicase inhibitor, immunomudulating agent, antioxydant agent, antibacterial agent or antisense agent.

115. The combination as defined in claim 114, wherein said additional agent is chosen from silybum marianum, interleukine-12, amantadine, ribozyme, thymosin, N-acetyl cysteine, cyclosporin, interferon α and ribavirin.

116. The combination as defined in anyone of claims 114 or 115, wherein said compound and said additionnal agent are administered sequentially.

- 117. The combination as defined in anyone of claims 114 or 115, wherein said compound and said additionnal agent are administered simultaneously.
- 118. A process for preparing a compound of formula A:

said process comprising the steps of adding:

- an enol ether;
- an hydride donating agent; and
- an organic carboxylic acid;

to a compound of formula B:

wherein,

 Y^1 is chosen from a bond, C_{2-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl;

Y is chosen from $COOR_{16}$, $COCOOR_{5}$, $P(O)OR_{2}OR_{5}$, $S(O)OR_{5}$, $S(O)_{2}OR_{5}$, tetrazole, $CON(R_{5})CH(R_{5})COOR_{5}$, $CONR_{10}R_{11}$, $CON(R_{5})-SO_{2}-R_{5}$, $CONR_{5}OH$

or halogen, wherein R_{s} , R_{s} , R_{10} and R_{11} are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C $_{2-12}$ alkynyl, C $_{4-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl, C $_{4-18}$ aralkyl; or R_{10} and R_{11} are taken together with the nitrogen to form a 3 to 10 membered heterocycle;

 $\rm R_a$ and $\rm R_b$ are each independently chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C $_{3-18}$ heteroaralkyl and C $_{6-18}$ aralkyl;

or R_a and R_b are taken together with the oxygens to form a 5 to 10 membered heterocycle;

 R_{16} is chosen from H, C $_{1-12}$ alkyl, C $_{2-12}$ alkenyl, C_{2-12} alkynyl, C $_{6-14}$ aryl, C $_{3-12}$ heterocycle, C_{3-18} heteroaralkyl and C_{6-18} aralkyl;

 R_1 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, C_{6-18} aralkyl or halogen;

 R_2 is chosen from C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl, or C_{6-18} aralkyl;

 R_3 is chosen from H, C_{1-12} alkyl, C_{2-12} alkenyl, C_{2-12} alkynyl, C_{6-14} aryl, C_{3-12} heterocycle, C_{3-18} heteroaralkyl or C_{6-18} aralkyl;

Z is chosen from H, halogen, C₁₋₆ alkyl.